ORIGINAL ARTICLE

Transcatheter or Surgical Treatment of Aortic-Valve Stenosis

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ABSTRACT

BACKGROUND

Among low-risk patients with severe, symptomatic aortic stenosis who are eligible for both transcatheter aortic-valve implantation (TAVI) and surgical aortic-valve replacement (SAVR), data are lacking on the appropriate treatment strategy in routine clinical practice.

METHODS

In this randomized noninferiority trial conducted at 38 sites in Germany, we assigned patients with severe aortic stenosis who were at low or intermediate surgical risk to undergo either TAVI or SAVR. Percutaneous- and surgical-valve prostheses were selected according to operator discretion. The primary outcome was a composite of death from any cause or fatal or nonfatal stroke at 1 year.

RESULTS

A total of 1414 patients underwent randomization (701 to the TAVI group and 713 to the SAVR group). The mean (±SD) age of the patients was 74±4 years; 57% were men, and the median Society of Thoracic Surgeons risk score was 1.8% (low surgical risk). The Kaplan–Meier estimate of the primary outcome at 1 year was 5.4% in the TAVI group and 10.0% in the SAVR group (hazard ratio for death or stroke, 0.53; 95% confidence interval [CI], 0.35 to 0.79; P<0.001 for noninferiority). The incidence of death from any cause was 2.6% in the TAVI group and 6.2% in the SAVR group (hazard ratio, 0.43; 95% CI, 0.24 to 0.73); the incidence of stroke was 2.9% and 4.7%, respectively (hazard ratio, 0.61; 95% CI, 0.35 to 1.06). Procedural complications occurred in 1.5% and 1.0% of patients in the TAVI and SAVR groups, respectively.

CONCLUSIONS

Among patients with severe aortic stenosis at low or intermediate surgical risk, TAVI was noninferior to SAVR with respect to death from any cause or stroke at 1 year. (Funded by the German Center for Cardiovascular Research and the German Heart Foundation; DEDICATE-DZHK6 ClinicalTrials.gov number, NCT03112980.)

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Transcatheter aortic-valve implantation (TAVI) is increasingly performed in patients with severe, symptomatic aortic-valve stenosis. In younger patients at low surgical risk, both TAVI and surgical aortic-valve replacement (SAVR) may be applicable, although the appropriate treatment strategy in this population remains subject to the considerations of individual heart teams.[1-3] On the basis of evidence from randomized clinical trials that have evaluated either balloon-expandable or self-expanding transcatheter heart valves, TAVI has evolved as a treatment option for younger and lower-risk patients and is increasingly used in clinical practice.[4-8] However, these trials were sponsored by industry and tested specific transcatheter heart-valve devices in selected patient populations, which limits the applicability of the results to inform routine clinical practice. Insufficient evidence remains regarding the comparison of TAVI and SAVR in a patient population mirroring the real-world setting in which operators have unrestricted access to several contemporary transcatheter heart-valve devices. A pragmatic clinical trial comparing TAVI with SAVR should allow for valve selection by the local heart team on the basis of individual patient anatomical and medical considerations after randomization to the treatment strategy.

To address these issues, we designed the pragmatic DEDICATE trial (Randomized, Multicenter, Event-Driven Trial of TAVI versus SAVR in Patients with Symptomatic Severe Aortic-Valve Stenosis) to compare the two procedures in patients who were at low or intermediate surgical risk and who were eligible for both treatment strategies in a real-world setting.

METHODS

TRIAL DESIGN

We performed this investigator-initiated, randomized trial at 38 German centers. A full list of participating sites is provided in Table S1 in the Supplementary Appendix, available with the full text of this article at NEJM.org.[9] The trial protocol and statistical analysis plan (available at NEJM.org) were designed by the principal and coordinating investigators, the steering committee, and the trial statisticians (Table S2). Data were collected at the trial sites, stored electronically at a central location, and analyzed by the trial statisticians.

The trial was conducted in compliance with the provisions of the Declaration of Helsinki and Good Clinical Practice guidelines. All the patients provided written informed consent. The University Medical Center Hamburg–Eppendorf coordinated the trial and is the legally responsible entity. The steering committee and an independent data and safety monitoring board provided trial oversight. The authors had unrestricted access to the data, prepared all drafts of the manuscript, and vouch for the completeness and accuracy of the data and for the fidelity of the trial to the protocol.

A Quick Take is available at NEJM.org

PATIENT SELECTION

Patients were eligible for inclusion in the trial if they had severe, symptomatic aortic stenosis, were at least 65 years of age, were considered to be at low or intermediate surgical risk according to clinical assessment, and were eligible for both TAVI and SAVR, as determined by the local interdisciplinary heart team. Patients with untreated and clinically significant coronary artery disease were excluded to avoid concomitant SAVR and coronary-artery bypass grafting, which is associated with an increased surgical risk. Patients who had undergone previous cardiac surgery, had bicuspid aortic-valve or other valvular heart disease, or had associated diseases warranting additional surgical treatment were also excluded. Details regarding complete inclusion and exclusion criteria are provided in the Supplementary Appendix. The representativeness of the trial population is shown in Table S3.

RANDOMIZATION AND PROCEDURES

Eligible patients underwent randomization by means of an electronic Web-based system in a 1:1 ratio to TAVI or SAVR with the use of balanced blocks of variable lengths, stratified according to the trial site and the Society of Thoracic Surgeons–Procedural Risk of Mortality (STS-PROM) score. On this scoring system (which ranges from 0 to 100%, with higher scores indicating a greater risk of death within 30 days

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after the procedure), low risk was defined as a score of 2% or less, intermediate risk as a score of more than 2 to 4%, and high risk as a score of more than 4%.

TAVI or SAVR was performed according to local best practices. All procedures were performed with the use of contemporary medical devices that had a European Certificate of Conformity (CE) mark, selected at the discretion of the heart team and operators. For TAVI procedures, a transfemoral-first vascular access strategy was advised; however, alternative access was also allowed. For SAVR procedures, surgical access (sternotomy or a minimally invasive approach) was permitted at the operator's discretion. Periprocedural management was performed according to local standards. Patients were evaluated at baseline, at the time of hospital discharge, and at 1 month and 1 year after the procedure.

OUTCOMES

The primary outcome was a composite of death from any cause or fatal or nonfatal stroke within 1 year after randomization. Key secondary outcomes were the components of the primary outcome along with acute kidney injury, arrhythmia and pacemaker implantation, bleeding, myocardial infarction, prosthetic-valve dysfunction, rehospitalization, and vascular complications. The definitions of the major secondary outcomes are provided in the protocol. An event-adjudication committee whose members were unaware of trial-group assignments assessed clinical events according to the updated definitions of the Valve Academic Research Consortium (VARC).[10] Echocardiographic images were assessed locally and reviewed by an independent core laboratory.

STATISTICAL ANALYSIS

We assumed an overall incidence of death from any cause or stroke of 6.2% in the two groups. (Details regarding the background for this assumption are provided in the Supplementary Appendix.) The noninferiority margin was a hazard ratio of 1.14, so the rejectable absolute between-group difference at 1 year was 1 percentage point. We determined that the enrollment of 1404 patients would provide the trial with a power of 80% to reject the noninferiority assumption at 1 year if the actual hazard ratio was 0.67 and the data censoring rate was 10% per year.

The primary analysis for determining the noninferiority of TAVI as compared with SAVR at 1 year after randomization was based on the upper boundary of the 95% confidence interval from a Cox regression analysis, with stratification according to the STS-PROM score for estimating the cause-specific hazard ratio with censoring at 1 year. Competing risk models were used to estimate cumulative incidence curves for secondary outcomes. The primary analysis was performed in the intention-to-treat population. Analyses of secondary outcomes were not adjusted for multiplicity, so the widths of the confidence intervals should not be used to infer treatment effects. A list of prespecified secondary and subgroup analyses and more detailed descriptions of the statistical analyses are provided in the Supplementary Appendix.

RESULTS

PATIENTS

From May 2017 through September 2022, a total of 1414 patients underwent randomization to either the TAVI group (701 patients) or the SAVR group (713 patients). In the TAVI group, 683 patients underwent the assigned treatment, 12 patients underwent SAVR, 4 patients withdrew from the trial, 1 patient was lost to follow-up, and 1 patient was found to be ineligible for the trial. In the SAVR group, 613 patients underwent the assigned treatment, 70 patients underwent TAVI, 26 patients withdrew from the trial, 2 were found to be ineligible for the trial, 1 patient was lost to follow-up, and 1 patient died before the index procedure (Fig. 1). The reasons for group crossover events are described in more detail in the Discussion section.

The baseline characteristics of the patients appeared to be balanced between the two groups (Table 1 and Table S4). The mean (±SD) age was 74±4 years; 790 (57%) of the patients were men, and the median STS-PROM score was 1.8%. Additional details regarding the distribution of ages and STS-PROM scores are provided in Figure S1.

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PROCEDURAL CHARACTERISTICS

The median time from randomization to the index procedure was 5 days. In the as-treated population, among the patients who underwent TAVI, 732 of 752 procedures (97.3%) were performed by means of transfemoral vascular access; 535 of 712 procedures (75.1%) were performed under local anesthesia or conscious sedation. A balloon-expandable transcatheter heart valve was implanted in 462 of 752 patients (61.4%), and a self-expanding transcatheter heart valve was implanted in 264 (35.1%). A cerebral embolic protection device was used in 38 of 738 procedures (5.1%). The median procedure time was 48 minutes (interquartile range, 35 to 65). Conversion to open-heart surgery was required in 6 patients, and 3 patients were treated with a second transcatheter heart valve. Immediate procedural complications occurred in 1.5% and 1.0% of patients in the TAVI and SAVR groups, respectively.

Among the patients who underwent SAVR, a full sternotomy was performed in 318 of 625 patients (50.9%) and partial sternotomy was performed in 242 (38.7%). In 99 patients (15.8%) who underwent SAVR, a sutureless rapid-deployment valve prosthesis was implanted, and 484 patients (77.4%) received a stented bioprosthesis. Concomitant operative procedures included coronary-artery bypass grafting in 11 patients (1.8%), replacement of the ascending aorta in 6 patients (1.0%), and mitral- or tricuspid-valve surgery in 3 patients (0.5%). The median procedure, cardiopulmonary bypass, and cross-clamp times were 165 minutes (interquartile range, 136 to 201), 88 minutes (interquartile range, 72 to 108), and 61 minutes (interquartile range, 50 to 75), respectively. Tables S5 and S6 and Figures S2 and S3 provide additional information about the procedures and the heart-valve prostheses.

The median length of stay in the intensive care unit was 1 day (interquartile range, 1 to 2) after TAVI and 2 days (interquartile range, 1 to 4) after SAVR; the median length of stay in the hospital after the procedure was 5 days (interquartile range, 4 to 7) and 9 days (interquartile range, 8 to 12), respectively. The number of patients who were discharged directly to home without an interval stay in a rehabilitation facility was 556 of 744 patients (74.7%) in the TAVI group and 252 of 624 (40.4%) in the SAVR group. Additional data regarding hospitalization and discharge, medications, and laboratory findings are provided in Tables S7, S8, and S9.

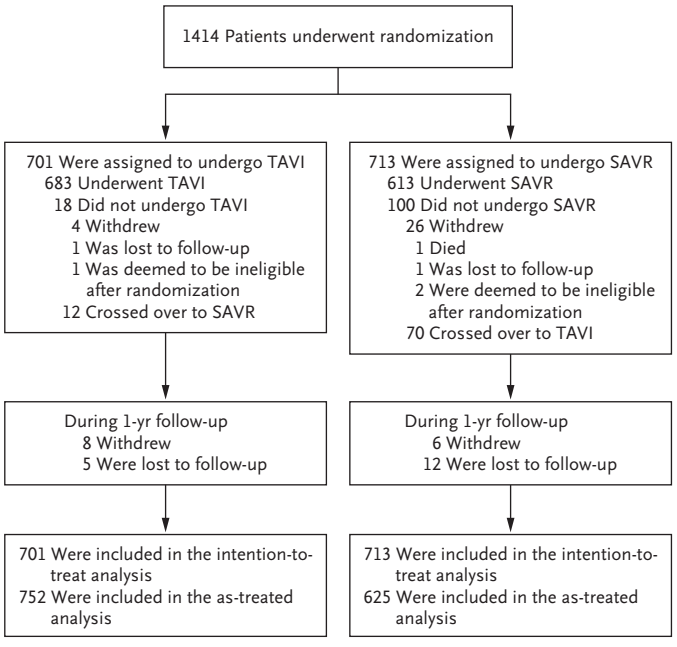

Figure 1. Randomization and Enrollment.

As part of the intention-to-treat trial design, 70 patients who had been assigned to receive surgical aortic-valve replacement (SAVR) were treated with transcatheter aortic-valve implantation (TAVI), mostly according to the patients' request. To account for this potential bias, the intention-to-treat analysis was followed by an as-treated analysis to evaluate the consistency of the results in the two populations. In the TAVI group, the as-treated population of 753 patients (with data available for 752 patients) included the 683 patients who had undergone TAVI and the 70 patients who had crossed over from the SAVR group. In the SAVR group, the as-treated population of 625 patients included the 613 patients who had undergone SAVR and the 12 patients who had crossed over from the TAVI group.

PRIMARY OUTCOME

The Kaplan–Meier estimate for the primary outcome, a composite of death from any cause or fatal or nonfatal stroke at 1 year in the intention-to-treat population, was 5.4% in the TAVI group and 10.0% in the SAVR group (hazard ratio, 0.53; 95% confidence interval [CI], 0.35 to 0.79; P<0.001 for noninferiority) (Fig. 2 and Table 2). Data for 30 days are shown in Table S10. In the as-treated population, the estimate for the primary outcome at 1 year was 5.6% in the TAVI

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Table 1. Characteristics of the Patients at Baseline (Intention-to-Treat Population).*

Characteristic	TAVI (N=701)	SAVR (N=713)
Demographic		
Age — yr	74.3±4.6	74.6±4.2
Male sex — no./total no. (%)	390/696 (56.0)	400/698 (57.3)
Medical history		
Median body-mass index (IQR)†	28.1 (25.3–31.9)	28.1 (25.4–31.2)
Median STS-PROM score (IQR) — %‡	1.8 (1.2–2.4)	1.9 (1.2–2.5)
Score on EuroSCORE II — %§	2.1±1.4	2.1±1.8
Median frailty score (IQR)¶	3.0 (2.0–4.0)	3.0 (2.0–3.0)
Left ventricular ejection fraction — %	57.8±9.8	57.7±9.3
Cardiovascular risk factors — no./total no. (%)		
Hypertension	588/694 (84.7)	605/694 (87.2)
Dyslipidemia	378/691 (54.7)	383/689 (55.6)
Diabetes mellitus	235/695 (33.8)	229/698 (32.8)
Coexisting illness — no./total no. (%)		
Coronary artery disease	238/694 (34.3)	266/697 (38.2)
Cerebrovascular disease	27/676 (4.0)	31/693 (4.5)
Peripheral vascular disease	34/694 (4.9)	45/697 (6.5)
Previous myocardial infarction	36/696 (5.2)	52/697 (7.5)
Previous stroke	42/692 (6.1)	42/696 (6.0)
Atrial fibrillation	201/695 (28.9)	191/697 (27.4)
COPD	101/695 (14.5)	118/697 (16.9)
Pulmonary hypertension	84/693 (12.1)	73/686 (10.6)
NYHA class ≥3	321/695 (46.2)	318/697 (45.6)
Permanent pacemaker	37/696 (5.3)	35/698 (5.0)
Left bundle-branch block	53/678 (7.8)	54/682 (7.9)
Right bundle-branch block	65/678 (9.6)	65/682 (9.5)

* Plus–minus values are means ±SD. For continuous variables, the median and interquartile range are presented for non-normally distributed variables. COPD denotes chronic obstructive pulmonary disease, IQR interquartile range, NYHA New York Heart Association, SAVR surgical aortic-valve replacement, and TAVI transcatheter aortic-valve implantation.
† The body-mass index is the weight in kilograms divided by the square of the height in meters.
‡ The Society of Thoracic Surgeons–Procedural Risk of Mortality (STS-PROM) score ranges from 0 to 100%, with higher scores indicating a greater risk of death within 30 days after the procedure.
§ The values on the European System for Cardiac Operative Risk Evaluation (EuroSCORE) II range from 0 to 100%, with higher scores indicating a greater risk of in-hospital death.
¶ Frailty was assessed according to the Clinical Frailty Scale, which ranges from 1 to 9, with higher scores indicating a patient population with an increased degree of frailty.

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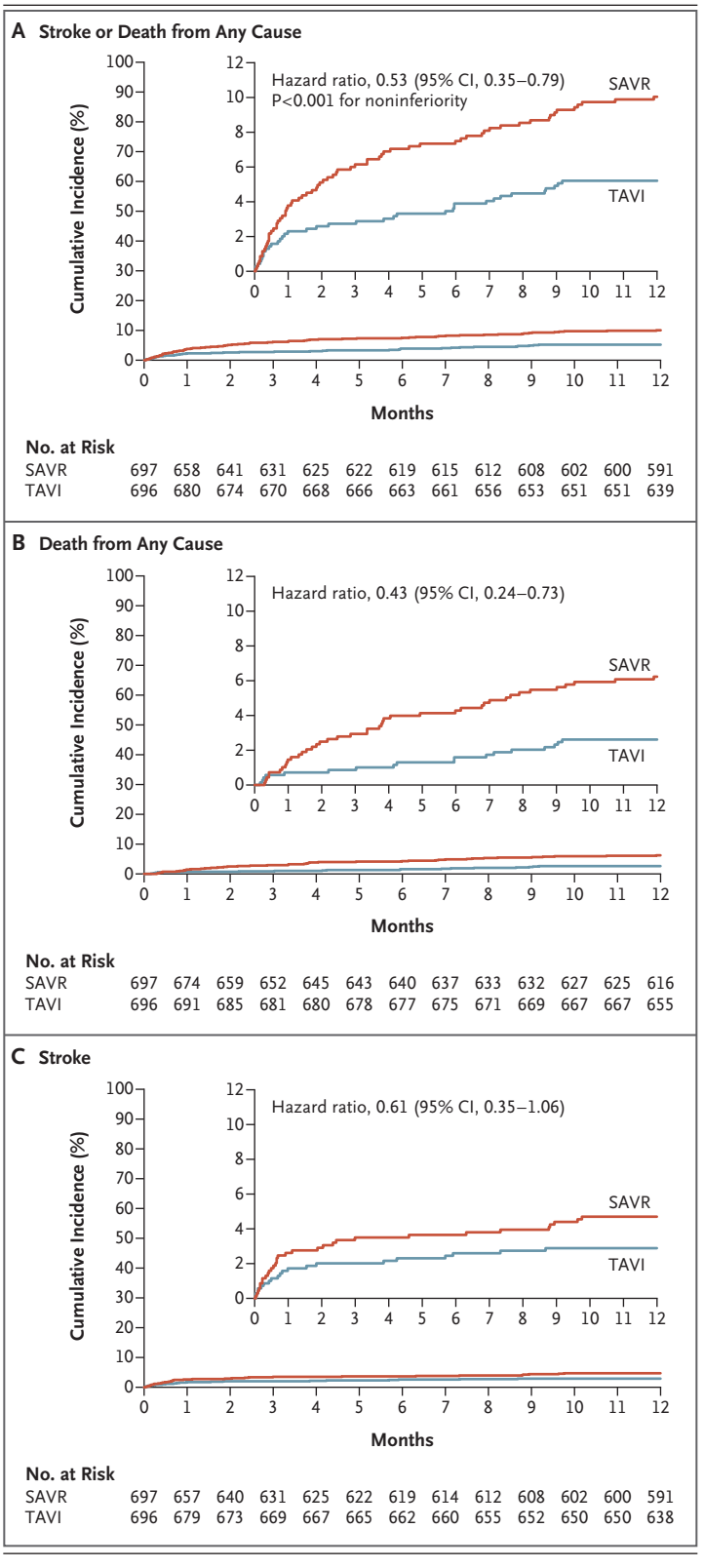
Figure 2. Death or Stroke (Composite Primary Outcome) and Its Components in the Intention-to-Treat Population.

Shown are Kaplan–Meier estimates (stratified according to the criteria of the Society of Thoracic Surgeons) of the risk of the primary outcome (Panel A) and its components, death from any cause (Panel B) and stroke (Panel C), among patients who underwent TAVI or SAVR. The insets show the same data on an expanded y axis.



group and 10.1% in the SAVR group (hazard ratio, 0.54; 95% CI, 0.36 to 0.80) (Table S11 and Fig. S7). The results of the subgroup analyses are shown in Figure 3.

SECONDARY OUTCOMES

At 1 year, the incidence of death from any cause was 2.6% in the TAVI group and 6.2% in the SAVR group (hazard ratio, 0.43; 95% CI, 0.24 to 0.73); the incidence of stroke was 2.9% and 4.7%, respectively (hazard ratio, 0.61; 95% CI, 0.35 to 1.06), and the incidence of stroke or transient ischemic attack was 4.1% and 5.1%, respectively (hazard ratio, 0.78; 95% CI, 0.47 to 1.27) (Table 2). The incidence of disabling stroke was 1.3% in the TAVI group and 3.1% in the SAVR group (hazard ratio, 0.42; 95% CI, 0.19 to 0.88); the incidence of death from any cause or disabling stroke was 3.8% and 8.4%, respectively (hazard ratio, 0.45; 95% CI, 0.28 to 0.70). Cardiovascular death occurred in 2.0% of the patients in the TAVI group and in 4.4% of those in the SAVR group (hazard ratio, 0.47; 95% CI, 0.24 to 0.86). All causes of death are listed in Table S13.

New-onset atrial fibrillation occurred in 12.4% of the patients in the TAVI group and in 30.8% of those in the SAVR group (hazard ratio, 0.36; 95% CI, 0.28 to 0.46); permanent pacemaker implantation was performed in 11.8% and 6.7% of the patients, respectively (hazard ratio, 1.81; 95% CI, 1.27 to 2.61). The incidence of prosthetic-valve dysfunction was 1.6% in the TAVI group and 0.6% in the SAVR group (hazard ratio, 2.44; 95% CI, 0.87 to 8.15). Event rates for aortic-valve reintervention, valve thrombosis, endocarditis, and cardiovascular rehospitalization were similar in the two groups at 1 year (Table 2). Overall, results from the as-treated analysis also

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Table 2. Primary and Secondary Outcomes at 1 Year (Intention-to-Treat Population).*

Outcome	TAVI (N=701)		SAVR (N=713)		Hazard Ratio (95% CI)
	no. of events	*% of patients*	*no. of events*	*% of patients*	
Primary outcome					
Death from any cause or stroke†	37	5.4	68	10.0	0.53 (0.35–0.79)
Secondary outcomes					
Death from any cause	18	2.6	42	6.2	0.43 (0.24–0.73)
Stroke	20	2.9	32	4.7	0.61 (0.35–1.06)
Stroke or TIA	28	4.1	35	5.1	0.78 (0.47–1.27)
Disabling stroke	9	1.3	21	3.1	0.42 (0.19–0.88)
Death from any cause or disabling stroke	26	3.8	57	8.4	0.45 (0.28–0.70)
Cardiovascular death	14	2.0	30	4.4	0.47 (0.24–0.86)
Myocardial infarction	7	1.0	14	2.1	0.51 (0.20–1.19)
New-onset atrial fibrillation	86	12.4	211	30.8	0.36 (0.28–0.46)
New-onset left bundle-branch block	222	32.0	120	17.5	2.03 (1.63–2.54)
New permanent pacemaker implantation	82	11.8	47	6.7	1.81 (1.27–2.61)
Prosthetic-valve dysfunction	11	1.6	4	0.6	2.44 (0.87–8.15)
Prosthetic-valve endocarditis	4	0.6	7	0.9	0.66 (0.18–2.19)
Prosthetic-valve thrombosis	5	0.7	2	0.3	2.09 (0.50–11.64)
Aortic-valve reintervention	4	0.6	2	0.3	1.70 (0.38–9.78)
Major or life-threatening or disabling bleeding	30	4.3	119	17.2	0.24 (0.16–0.35)
Acute kidney injury of stage II or III‡	9	1.3	17	2.5	0.56 (0.24–1.21)
Vascular access-site complication	55	7.9	5	0.7	10.64 (4.84–28.94)
Rehospitalization for cardiovascular cause	84	12.2	91	13.3	0.89 (0.66–1.20)

* The analyses were stratified according to the STS-PROM score. The percentage of patients was calculated as a Kaplan–Meier estimate. The 95% confidence intervals have not been adjusted for multiplicity and should not be used to make hypothesis-test inferences about superiority or noninferiority. TIA denotes transient ischemic attack.
† P<0.001 for the primary analysis.
‡ Acute kidney injury was adjudicated according to Valve Academic Research Consortium 2 criteria within 7 days after the index procedure.

appeared to be consistent with the results from the intention-to-treat analysis (Table S11 and Fig. S7).

Aortic-valve hemodynamics from baseline to hospital discharge and at 1 year are shown in Figures S4, S5, and S6. At 1 year, the mean aortic-valve gradients were 10 mm Hg (95% CI, 8 to 14) in the TAVI group and 11 mm Hg (95% CI, 8 to 14) in the SAVR group. The mean effective orifice area was 1.6 cm^2 (95% CI, 1.4 to 2.0) in the TAVI group and 1.6 cm^2 (95% CI, 1.3 to 1.9) in the SAVR group. The number of patients with at least moderate regurgitation at 1 year was 16 (2.8%) and 5 (1.0%) in the TAVI and SAVR groups, respectively (Table S14). The results of the 6-minute

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walk test are provided in Figure S8, and quality-of-life survey results are provided in Table S15.

SAFETY

The incidence of major or life-threatening bleeding was 4.3% in the TAVI group and 17.2% in the SAVR group (hazard ratio, 0.24; 95% CI, 0.16 to 0.35); the incidence of vascular access-site complications was 7.9% and 0.7%, respectively (hazard ratio, 10.64; 95% CI, 4.84 to 28.94). Acute kidney injury of stage II or III occurred in 1.3% of the patients in the TAVI group and in 2.5% of those in the SAVR group (hazard ratio, 0.56; 95% CI, 0.24 to 1.21); myocardial infarction occurred in 1.0% and 2.1%, respectively (hazard ratio, 0.51; 95% CI, 0.20 to 1.19) (Table 2).

DISCUSSION

In this investigator-initiated, randomized trial of TAVI as compared with SAVR involving patients with severe, symptomatic aortic-valve stenosis who were at low or intermediate surgical risk, we found that TAVI was noninferior to SAVR with respect to death from any cause or fatal or nonfatal stroke at 1 year (the composite primary outcome). The annual event rates for the primary outcome and the majority of secondary outcomes appeared to be consistently lower among the patients who had undergone TAVI than among those who had undergone SAVR. In this trial, which was performed without industry sponsorship, we enrolled a population that was similar to the patients in standard clinical practice in many Western countries. Periprocedural treatment management, including the selection of valve prostheses, was determined by the local heart team and reflected contemporary treatment of aortic-valve stenosis.

On the basis of the results of trials investigating TAVI and SAVR that enrolled patients at low surgical risk, the use of TAVI in the community has expanded to include patients at low operative risk and younger ages, treatment that has exceeded the recommendations in current treatment guidelines.[1,2,4,6,8,11-13] However, the generalizability of the findings of randomized clinical trials to clinical practice had been limited because of the strict selection criteria for patient inclusion and the study of specific transcatheter heart-valve prostheses in each trial. In our trial, we enrolled patients who were at low or intermediate surgical risk, a choice that was confirmed by the median STS-PROM score and mean age of the patients. These measures are consistent with those of the PARTNER 3[4] and Evolut Low Risk[6] trials that enrolled low-risk patients but differ from those in the populations enrolled in the earlier NOTION[12] and UK TAVI[11] trials. In our trial, the local heart team evaluated all the patients and agreed on the inclusion of patients according to their suitability for both SAVR and TAVI. We also observed that there were differences in the operator's choice of contemporary valve prostheses and periprocedural management, thus emphasizing the importance of large pragmatic trials to evaluate treatment strategies.

A recent meta-analysis of major randomized trials that included low-risk patients showed an early benefit for TAVI with respect to death or disabling stroke.[14] In our trial, the incidence of the primary and secondary outcome events after SAVR were higher than anticipated and exceeded those reported in recent registries.[15] The frequencies of death and stroke at 1 year in the SAVR group were also notably higher than those observed in recent trials of TAVI as compared with SAVR among low-risk patients, despite the occurrence of a similar incidence of perioperative complications.[4,6] One explanation is that in our trial a large proportion of patients were recruited during the coronavirus disease 2019 (Covid-19) pandemic, which has been associated with worse outcomes after cardiac surgery.[16] Another explanation is that we enrolled an increased proportion of women, and female sex has been associated with higher mortality after SAVR in previous studies.[17] The risk of death from any cause or stroke in our trial was similar to that in the PARTNER 3 trial.[4] The results of our analyses of other secondary outcomes in the TAVI and SAVR groups were also in line with the findings of previous studies.[14] Aortic-valve reintervention, valve thrombosis, or endocarditis occurred in less than 1% of patients in the two treatment groups. The apparently higher rates of residual aortic regurgitation among patients who underwent TAVI merit longer-term follow-up. Other studies have not shown a higher likelihood of early bioprosthetic-valve failure after TAVI when patients were followed for 8 years.[5,7,18-20]

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Subgroup	TAVI	SAVR	Hazard Ratio for Death or Stroke (95% CI)
	no. of patients with event/total no.		
Overall	37/701	68/713	0.53 (0.35–0.79)
Age			
<75 yr	18/359	30/345	0.56 (0.31–0.98)
≥75 yr	19/337	38/354	0.51 (0.29–0.87)
Sex			
Male	21/390	35/400	0.60 (0.35–1.02)
Female	16/306	33/298	0.46 (0.25–0.81)
Body-mass index			
<25	8/163	17/159	0.46 (0.19–1.01)
25 to <30	12/277	26/293	0.48 (0.24–0.92)
≥30	17/255	25/246	0.63 (0.34–1.15)
STS-PROM score			
≤2%	15/387	23/378	0.62 (0.32–1.18)
>2 to ≤4%	18/282	36/284	0.49 (0.27–0.84)
>4%	4/27	9/35	0.53 (0.15–1.55)
NYHA class			
≤2	20/374	30/379	0.66 (0.37–1.16)
>2	17/321	38/318	0.42 (0.23–0.73)
Coronary artery disease			
Yes	15/238	26/266	0.62 (0.32–1.14)
No	22/456	42/431	0.48 (0.28–0.80)
Previous myocardial infarction			
Yes	1/36	7/52	0.27 (0.03–1.23)
No	36/660	61/645	0.56 (0.37–0.83)
Previous stroke			
Yes	2/42	5/42	0.44 (0.08–1.82)
No	35/650	62/654	0.55 (0.36–0.82)
Cerebrovascular disease			
Yes	2/27	6/31	0.42 (0.08–1.63)
No	35/649	60/662	0.57 (0.38–0.86)
Peripheral vascular disease			
Yes	2/34	6/45	0.48 (0.09–1.89)
No	35/660	61/652	0.55 (0.36–0.82)
COPD			
Yes	4/101	15/118	0.32 (0.10–0.85)
No	33/594	52/579	0.60 (0.38–0.92)
Left ventricular ejection fraction			
<55%	7/165	18/179	0.42 (0.17–0.94)
≥55 to <60%	11/165	18/181	0.66 (0.31–1.36)
≥60%	19/336	29/306	0.58 (0.32–1.02)
Aortic-valve mean gradient			
<40 mm Hg	11/243	33/291	0.37 (0.18–0.70)
≥40 mm Hg	26/458	35/422	0.67 (0.40–1.11)
Glomerular filtration rate			
<60 ml/min/1.73 m^2	13/210	33/194	0.34 (0.18–0.63)
≥60 ml/min/1.73 m^2	23/469	35/493	0.67 (0.40–1.13)
Covid-19 lockdown at admittance			
Yes	1/38	5/40	0.28 (0.03–1.42)
No	36/663	63/673	0.53 (0.35–0.79)
Date of randomization			
Before March 1, 2020	18/374	32/365	0.53 (0.29–0.93)
On or after March 1, 2020	19/327	36/348	0.53 (0.30–0.91)

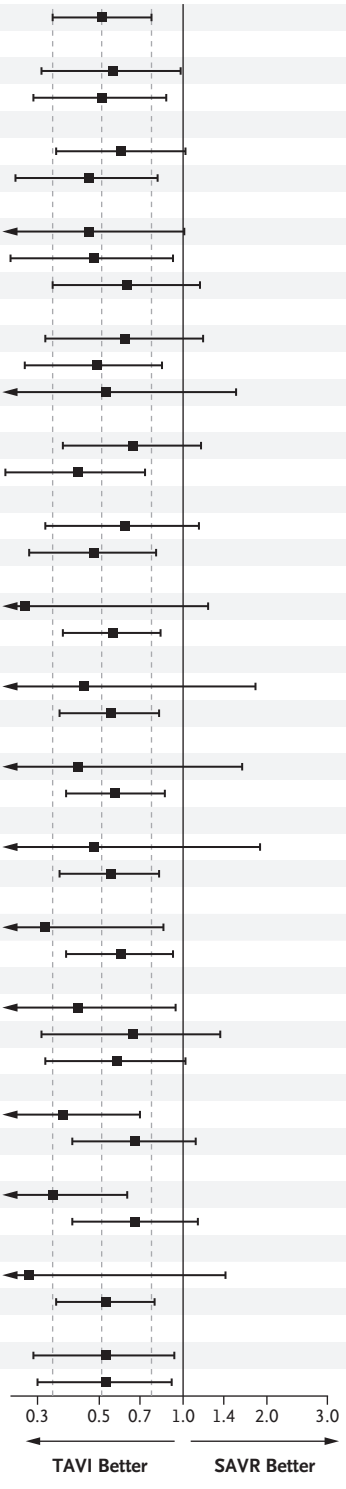

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Figure 3 (facing page). Subgroup Analyses of the Primary Outcome.

All subgroup analyses were performed with the use of unadjusted Cox regression according to time to event in the intention-to-treat population with 1 year of follow-up. The dashed lines indicate the hazard ratio and 95% confidence interval in the overall trial population. COPD denotes chronic obstructive pulmonary disease, Covid-19 coronavirus disease 2019, NYHA New York Heart Association, and STS-PROM Society of Thoracic Surgeons–Procedural Risk of Mortality.

Long-term follow-up of the DEDICATE trial population will help to determine whether early primary outcome effects will translate into long-term benefits.

Our trial has several limitations. First, the prespecified noninferiority analyses were limited to 1 year of follow-up. Therefore, the current analyses cannot be extrapolated to long-term outcomes; the primary outcome will be reevaluated at 5 years. Second, as part of the intention-to-treat trial design in this pragmatic trial, 70 patients who had been assigned to receive SAVR were treated with TAVI, mostly according to the patients' request. To account for this potential bias, we performed an intention-to-treat analysis, followed by an as-treated analysis, to evaluate the consistency of the results in the two populations. Third, we excluded patients with bicuspid valves and those who required concomitant surgery in order to evaluate a uniform patient population. However, as the indications for TAVI expand toward younger patients, more patients with bicuspid aortic valves will receive TAVI. Fourth, the trial was conducted during the Covid-19 pandemic, which may have had an effect on the overall diagnostic and treatment pathways. However, subgroup analyses that were stratified according to hospital admission during the Covid-19 lockdown appeared to provide similar results. Fifth, because the majority of patients had already been enrolled at the time of publication of the third updated version of VARC criteria,[21] we proceeded with clinical-event adjudication according to the VARC-2 document.[10] Sixth, the trial does not describe a consecutive all-comers population because some patients requested a specific therapy and were not included in the trial. However, no bias was observed in treatment assignments in our trial as compared with the respective overall German patient population with respect to age and sex, as documented in the German Heart Report.[22] Seventh, the trial was conducted only in Germany and we did not collect data with respect to race or ethnic group, so the results may not be uniformly generalizable.

Our trial also has several strengths. The unrestricted operator's choice of transcatheter heart valves that were used in the trial was driven by the patients' anatomical characteristics and local medical considerations. This tailored approach may have improved results achieved with TAVI in the DEDICATE trial, both in the intention-to-treat and the as-treated analysis. The event-adjudication committee assessed clinical events in a blinded fashion to ensure unbiased evaluation. Finally, the trial was funded by academic research organizations and performed independent of industry funding.

Among patients with severe aortic stenosis at low or intermediate surgical risk, TAVI with prosthesis selection based on operator discretion was noninferior to SAVR with respect to the risk of death from any cause or stroke at 1 year.

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

A data sharing statement provided by the authors is available with the full text of this article at NEJM.org.

APPENDIX

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