

Risk-Adjusted Comparison of In-Hospital Outcomes of Transcatheter and Surgical Aortic Valve Replacement

Peter Stachon, MD;* Klaus Kaier, PhD;* Andreas Zirlík, MD; Wolfgang Bothe, MD; Timo Heidt, MD; Manfred Zehender, MD; Christoph Bode, MD; Constantin von zur Mühlen, MD

Background—Transfemoral transcatheter aortic valve replacement (TF-TAVR) is recommended for patients suffering from aortic valve stenosis at increased operative risk. Beyond that, patients with different comorbidities could benefit from TF-TAVR. The present study compares real-world in-hospital outcomes of surgical aortic valve replacement and TF-TAVR.

Methods and Results—For all 33 789 isolated TF-TAVR and surgical aortic valve replacement procedures performed in Germany in 2014 and 2015, comorbidities and in-hospital outcomes were identified by *International Classification of Diseases (ICD)*- and OPS (Operation and procedure key)-codes. Patients undergoing TF-TAVR were older and at increased estimated risk. Outcomes were risk-adjusted to allow comparison. TF-TAVR was associated with a lower risk for acute kidney injuries (odds ratio [OR] 0.62, $P<0.001$), for bleeding (OR 0.17, $P<0.001$), and for prolonged mechanical ventilation (>48 hours, OR 0.21, $P<0.001$). Risk for stroke was similar (OR 1.07, $P=0.558$). As expected, the risk for pacemaker implantations was higher after TF-TAVR (OR 4.61, $P<0.001$). In all patients, none of the treatment strategies had a clear advantage on the risk for in-hospital mortality (OR 0.83, $P=0.068$). However, in patients aged >80 years and at high operative risk undergoing TF-TAVR in-hospital mortality was lower (TF-TAVR versus surgical aortic valve replacement 80–84, OR 0.55; $P=0.002$; ≥ 85 years, OR 0.42, $P=0.006$; EuroSCORE (European System for Cardiac Operative Risk Evaluation) >9: OR 0.62, $P=0.001$). TF-TAVR was superior in patients with renal failure and in NYHA (New York Heart Association)-Class III/IV. Other risk groups were not found to be factors favoring a treatment strategy.

Conclusions—The present study indicates a superiority of TF-TAVR in clinical practice for patients at increased operative risk, aged >80 years, in NYHA-Class III/IV, and with renal failure. (*J Am Heart Assoc.* 2019;8:e011504. DOI: 10.1161/JAHA.118.011504.)

Key Words: aortic stenosis • aortic valve • surgery • transcatheter aortic valve • transcatheter aortic valve implantation

The first transcatheter aortic valve replacement (TAVR) was performed in 2002 in a patient with severe aortic stenosis suffering from cardiogenic shock unsuited for

surgical aortic valve replacement (SAVR) because of a critical perioperative state.¹ During the following years, TAVR became an alternative for inoperable patients suffering from aortic valve stenosis. After 5 years of development and trials, 2 valves received the European certification for application in humans. These valves showed non-inferiority to SAVR in 2 randomized controlled trials with patients at extreme or high operative risk.^{2,3} Consequently, guidelines adopted TAVR as a treatment option for patients with severe aortic valve stenosis at high operative risk.⁴ TAVR procedures soon outnumbered SAVR in clinical practice.⁵ Advances in transcatheter technology and learning effects over time further improved results after TAVR.⁶ Several large registries proved that the convincing results from randomized controlled trials are transferable into clinical practice.^{7–9} Subsequently, 2 randomized controlled trials compared TAVR and SAVR in patients at intermediate operative risk and demonstrated non-inferiority of TAVR after 2 years of follow-up.^{10,11} Transfemoral TAVR (TF-TAVR) with a balloon-expandable valve was even superior to SAVR

From the University Heart Center Freiburg, Department of Cardiology and Angiology I, Faculty of Medicine (P.S., K.K., A.Z., T.H., M.Z., C.B., C.v.z.M.), Institute of Medical Biometry and Medical Informatics, University Medical Center Freiburg, Faculty of Medicine (K.K.), and Department of Cardiac and Vascular Surgery, Heart Center Freiburg, Faculty of Medicine, (W.B.) University of Freiburg, Freiburg, Germany; Department of Cardiology, University Hospital Graz, Austria (A.Z.).

Accompanying Tables S1 through S17 and Figures S1 and S2 are available at <https://www.ahajournals.org/doi/suppl/10.1161/JAHA.118.011504>

*Dr Stachon and Dr Kaier are co-first authors.

Correspondence to: Peter Stachon, MD, University Heart Center Freiburg, Cardiology and Angiology I, Hugstetter Str. 55, 79106 Freiburg, Germany. E-mail: peter.stachon@universitaets-herzzentrum.de

Received November 22, 2018; accepted February 15, 2019.

© 2019 The Authors. Published on behalf of the American Heart Association, Inc., by Wiley. This is an open access article under the terms of the Creative Commons Attribution-NonCommercial License, which permits use, distribution and reproduction in any medium, provided the original work is properly cited and is not used for commercial purposes.

Clinical Perspective

What Is New?

- We analyzed >33 000 real-world aortic valve replacements and identified subgroups which benefit from transfemoral transcatheter aortic valve replacement.
- In all subgroups, patients undergoing transfemoral transcatheter aortic valve replacement had lower adjusted risk for acute kidney injuries, lower risk of bleeding, and lower risk for prolonged mechanical ventilation compared with patients undergoing surgical aortic valve replacement.
- The risk for in-hospital mortality was lower in patients at increased operative risk, aged >80 years, in patients with advanced kidney failure, and in highly symptomatic patients.

What are the Clinical Implications?

- Results from randomized controlled trials are transferable into clinical practice.
- Transfemoral transcatheter aortic valve replacement should be preferentially considered in patients at increased operative risk, aged >80 years, with advanced kidney failure, and highly symptomatic.

in a propensity-matched analysis.¹² These results led to a further modification of the guidelines: TAVR is now recommended for patients at intermediate or high operative risk.¹³ Nevertheless, risk scores are not the only criteria for the decision between SAVR and TAVR: SAVR remains the preferred method for patients aged <75 years, since there are concerns about the durability of transcatheter valves. On the other hand, TAVR is recommended in case of severe comorbidities which are not adequately reflected by risk scores.¹³ Data from randomized controlled trials or large registries comparing both treatment strategies in younger patients or in patients with distinct comorbidities are still lacking. This may be because of limited cohort sizes in studies and resulting difficulties in obtaining statistically significant results for subgroups. However, breaking down the outcomes achieved by patients treated with the various approaches by patient subgroup is vital to provide an empirical basis for clinical practice, which is faced with a highly diverse patient population. For an accurate estimation of treatment effects within subgroups, estimates from observational databases can complement randomized controlled trials.¹⁴ This is particularly true for subgroups for which randomized controlled trials are not feasible because of financial constraints.

The aim of the present study is to perform subgroup analyses for a variety of at-risk populations with sufficient patient numbers to achieve conclusive results. To this end, we analyzed the records of 33 789 SAVR or TF-TAVR

procedures performed in Germany between 2014 and 2015 on the basis of *International Classification of Diseases (ICD)* and OPS (Operation and procedure key) codes.

Methods

Data Acquisition

Since 2005, data on all hospitalizations in Germany have been available for scientific use via the Diagnosis Related Groups statistics collected by the Research Data Center of the Federal Bureau of Statistics (DESTATIS). These hospitalization data, including diagnoses and procedures, are a valuable source of representative nationwide data on the in-hospital treatment of patients. This database represents a virtually complete collection of all hospitalizations in German hospitals that are reimbursed according to the Diagnosis Related Groups system. From this database, we extracted data on 33 789 cases of isolated SAVR and TF-TAVR procedures conducted in 2014 or 2015. As described previously, patients with a baseline diagnosis of pure aortic regurgitation (main or secondary diagnosis other than I35.0, I35.2, I06.0, I06.2) and those with concomitant cardiac surgery or percutaneous coronary intervention were not included in this analysis.⁵ A complete list of procedure codes as well as a more detailed discussion of the validity of the data source may be found in Table S1.

Our study did not involve direct access by the investigators to data on individual patients but only access to summary results provided by the Research Data Center. Therefore, approval by an ethics committee and informed consent were determined not to be required, in accordance with German law. All summary results were anonymized by DESTATIS. In practice, this means that any information allowing the drawing of conclusions about a single patient or a specific hospital was censored by DESTATIS to guarantee data protection. Moreover in order to prevent the possibility to draw conclusions to a single hospital, the data are verified and situationally censored by DESTATIS in those cases.

Definition of End Points

The analysis focuses on 7 different end points: in-hospital mortality, stroke, acute kidney injury, bleeding events, ventilator therapy of >48 hours, permanent pacemaker implantation, and length of hospital stay. Stroke and acute kidney injury were defined using *ICD, Tenth Revision (ICD-10)* codes (secondary diagnosis I63* or I64 and N17*, respectively). Bleeding was defined as requiring a transfusion of <5 units of red blood cells and defined using OPS-codes (8-800.c1 to 8-800.cr), as was the case for permanent pacemaker implantation (5-377.0 to 5-377.7). In-hospital mortality, length of mechanical ventilation, and length of hospital stay were part of DESTATIS' main set of variables. For

Table 1. Baseline Characteristics in SAVR and TF-TAVR Performed in 2014 and 2015. *p*-Values are calculated using the students *t*-test (age, EuroSCORE) or chi-square test

	SAVR (n=13 151)		TF-TAVR (n=20 638)		<i>P</i> Value
Logistic EuroSCORE, mean/SD	5.30	4.66	13.91	10.29	<0.001
Age in y, mean/SD	68.53	10.04	81.12	6.03	<0.001
Women, n %	5057	38.45%	11 251	54.52%	<0.001
NYHA II, n %	1745	13.27%	2020	9.79%	<0.001
NYHA III or IV, n %	3746	28.48%	9572	46.38%	<0.001
CAD, n %	2525	19.20%	9760	47.29%	<0.001
Hypertension, n %	8091	61.52%	13 029	63.13%	0.003
Previous MI within 4 mo, n %	68	0.52%	297	1.44%	<0.001
Previous MI within 1 y, n %	38	0.29%	135	0.65%	<0.001
Previous MI after 1 y, n %	256	1.95%	804	3.90%	<0.001
Previous CABG, n %	248	1.89%	1895	9.18%	<0.001
Previous cardiac surgery, n %	656	4.99%	2960	14.34%	<0.001
Peripheral vascular disease, n %	598	4.55%	1835	8.89%	<0.001
Carotid disease, n %	478	3.63%	1032	5.00%	<0.001
COPD, n %	1189	9.04%	2711	13.14%	<0.001
Pulmonary hypertension	1330	10.11%	4286	20.77%	<0.001
Renal disease, GFR <15, n %	117	0.89%	460	2.23%	<0.001
Renal disease, GFR <30, n %	171	1.30%	911	4.41%	<0.001
Atrial fibrillation, n %	5246	39.89%	9266	44.90%	<0.001
Diabetes mellitus, n %	3311	25.18%	6735	32.63%	<0.001

CABG indicates coronary artery bypass graft; CAD, coronary artery disease; COPD, chronic obstructive pulmonary disease; EuroSCORE, European System for Cardiac Operative Risk Evaluation; GFR, glomerular filtration rate; MI, myocardial infarction; NYHA, New York Heart Association; SAVR, surgical aortic valve replacement; TF-TAVR, transfemoral transcatheter aortic valve replacement.

all other comorbidities, the existing anamnestic or acute distinctive codes were used (we have discussed OPS and ICD codes in detail previously⁵). For calculation of the estimated logistic EuroSCORE (European System for Cardiac Operative Risk Evaluation), we were able to populate all fields except for critical preoperative state and left ventricular function. In these, we assumed an inconspicuous state (i.e, no critical preoperative state and no left ventricular dysfunction) and thus calculated a best-case scenario. To allow a direct comparison of the baseline risk factor composition between TAVR and SAVR patients, we calculated logistic EuroSCORE values assuming isolated SAVR procedures for both groups.

Statistical Analysis

The primary outcome was in-hospital mortality. Secondary outcomes include post-procedural complications such as stroke and bleeding events (transfusion of ≥ 5 red blood cells), as well as the proportion of patients with ventilator therapy >48 hours and permanent pacemaker implantation.

In a previous study, Reinohl et al⁵ identified 20 baseline patient characteristics to describe risk profiles between

procedural groups. Since patients were not randomized to the 2 treatment options (TF-TAVR or SAVR), logistic or linear regression models were used with these 20 baseline patient characteristics included as potential confounders (all covariates listed in Table 1). Year 2015 was added as an additional confounder to improve the precision of the estimates. To account for the correlation of error terms of patients treated in the same hospital, a random intercept was included at the center level.

To identify subgroups of patients in which 1 of the 2 treatment options (TF-TAVR or SAVR) might be preferable with respect to a specific outcome, a number of subgroups of interest were predefined: age groups, preoperative risk assessed by the EuroSCORE, female sex, heart failure (New York Heart Association [NYHA] III or IV), previous coronary artery bypass graft (CABG), peripheral vascular disease, chronic obstructive pulmonary disease (COPD), pulmonary hypertension, renal failure (glomerular filtration rate <30), and diabetes mellitus.

If the respective outcome rarely occurs within these subgroups there may not be enough data with which to model the relationship between the outcome and all potential confounders.¹⁵ Therefore, an additional propensity approach

was applied within the different subgroups. First, a logistic regression model was performed on the same patient and procedural characteristics to calculate the propensity score for each patient within the different subgroups. The propensity score represents the likelihood that the patient was in the TF-TAVR arm. Please note that the outcome variables were not used in this step. Then, propensity score adjustment was applied using the propensity score as continuous covariate.¹⁶ Again, logistic regression models with a random intercept at the center level were conducted.

As a result, each outcome was analyzed twice for each subgroup: once using covariate adjustment and once using propensity score adjustment. However, analyses using regression adjustment are shown as base case analyses. In the light of an ongoing discussion that covariate adjustment models might be overfitted when the number of covariates is large compared with the number of patients or outcome events, results of analyses using propensity score adjustment are compared with those from covariate adjustment when there were few events per confounder in the respective subgroup and outcome. See Figure S1 and Tables S2 through S17 for results of the different regression analyses.

All analyses were performed by using Stata 14 (StataCorp, College Station, Texas, USA).

Results

Patients

Between January 2014 and December 2015, 13 151 isolated SAVR and 20 638 TF-TAVR procedures were performed in 102 different centers in Germany.

Patients undergoing TF-TAVR were more likely to be women (female sex SAVR: 38.5%; TF-TAVR 54.5%), were older (SAVR: 68.5 years; TF-TAVR 81.1 years), and had more comorbidities: They suffered significantly more frequently from coronary artery disease, atrial fibrillation, carotid disease, COPD, pulmonary hypertension, renal disease, and diabetes mellitus. Furthermore, patients undergoing TF-TAVR had more symptoms from aortic stenosis, 46% being in NYHA Class III or IV compared with 28% of patients treated with SAVR. The share of patients with previous cardiac surgery was higher in patients undergoing TF-TAVR (SAVR: 5.0%; TF-TAVR 14.3%). Consequently, the estimated operative risk was substantially higher in patients treated with TF-TAVR (EuroSCORE SAVR: $5.3 \pm 4.7\%$; $P < 0.001$; TF-TAVR: $13.9 \pm 10.3\%$, Table 1).

Unadjusted In-Hospital Outcomes

Unadjusted outcomes differed between patients treated with SAVR and TF-TAVR. In comparison with previous years, in-hospital mortality is low, with 2.0% after SAVR and 3.2% after TF-TAVR, respectively ($P < 0.001$).⁵ Besides the lower mortality

Table 2. In-Hospital Outcomes in SAVR and TF-TAVR Performed in 2014 and 2015

	SAVR		TF-TAVR		Unadjusted Comparison
	n	Rate	n	Rate	P Value
In-hospital mortality	262	1.99%	667	3.23%	<0.001
Stroke	213	1.62%	500	2.42%	<0.001
Acute kidney injury	637	4.84%	1144	5.54%	0.006
Bleeding >5 units	1245	9.47%	673	3.26%	<0.001
Mechanical ventilation >48 h	921	7.00%	607	2.94%	<0.001
New permanent pacemaker	527	4.01%	3492	16.92%	<0.001
Length of hospital stay, mean SD	14.73	9.55	14.90	9.66	0.123

P values are calculated using the Chi-square test or the students *t* test (length of hospital stay). SAVR indicates surgical aortic valve replacement; TF-TAVR, transfemoral transcatheter aortic valve replacement.

rate, SAVR was also associated with fewer strokes (SAVR: 1.6%; TF-TAVR: 2.4%, $P < 0.001$), acute kidney injuries (SAVR: 4.8%; TF-TAVR: 5.5%, $P = 0.006$), and pacemaker implantations (SAVR: 4.0%; TF-TAVR: 16.9%, $P < 0.001$). On the other hand, bleeding (>5 units of red blood cells, SAVR: 9.5%; TF-TAVR: 3.3%, $P < 0.001$), and prolonged mechanical ventilation rates (>48 hours, SAVR: 7.0%; TF-TAVR: 2.9%, $P < 0.001$) were higher among SAVR patients (Table 2). Unadjusted length of hospital stay was comparable for SAVR and TF-TAVR patients (14.7 and 14.9 days, $P = 0.123$).

Risk-Adjusted Outcomes

After risk adjustment, the effect of treatment selection on in-hospital outcomes was slightly different: In-hospital mortality and stroke were similar (TF-TAVR compared with SAVR mortality: OR 0.83, $P = 0.068$, stroke OR 1.07, $P = 0.558$) in the entire population. However, TF-TAVR was associated with a lower risk for acute kidney injuries (OR 0.62, $P < 0.001$), for bleeding (OR 0.17, $P < 0.001$), and for prolonged ventilation (OR 0.21, $P < 0.001$). As expected, patients undergoing TF-TAVR had an increased risk for pacemaker implantations even after risk adjustment (OR 4.61, $P < 0.001$, Figure 1). In addition, TF-TAVR was associated with a shorter length of hospital stay (-1.33 days, $P < 0.001$).

Risk-Adjusted Mortality in Different Subgroups

Although guidelines in 2014 and 2015 recommended TAVR for patients at high operative risk, a remarkable share of

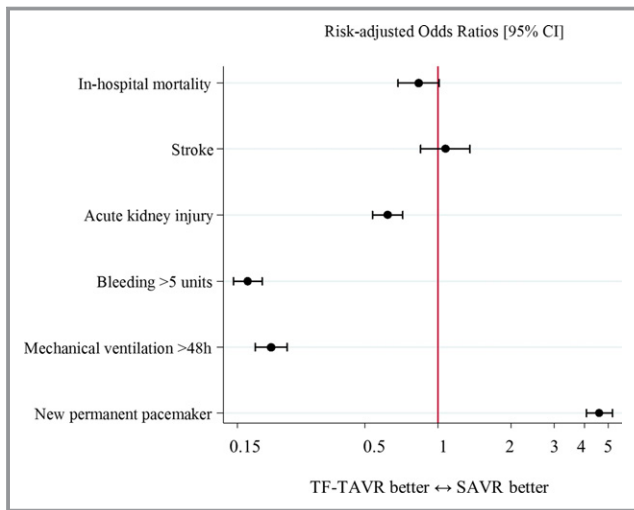


Figure 1. Risk-adjusted in-hospital outcomes in SAVR and TF-TAVR performed in 2014 and 2015. Results of multivariate logistic regression analyses with 20 predefined baseline patient characteristics included as potential confounders (all covariates listed in Table 1). SAVR indicates surgical aortic valve replacement; TF-TAVR, transfemoral transcatheter aortic valve replacement.

patients undergoing TF-TAVR were <75 years or at intermediate or low operative risk in clinical practice. The outcomes of SAVR and TF-TAVR differed in those subgroups (Table 3). To identify subgroups of patients who benefited from either SAVR or TF-TAVR, we analyzed outcomes in different predefined subgroups.

Risk for mortality differed between the subgroups: among the younger patients with an age <75 years, SAVR was the most common treatment strategy. The mortality was 1.5% after SAVR and 2.5% after TF-TAVR, but was not significantly different after risk adjustment (OR 0.85, $P=0.404$). The same is true for the group of patients aged 75 to 79 years, where TF-TAVR procedures outnumbered SAVR, but effect of treatment selection on in-hospital mortality was again not significant (OR 0.82, $P=0.219$). In patients >80 years, TF-TAVR was the preferential treatment strategy. In these older patients, TF-TAVR was associated with a significantly lower risk for in-hospital mortality (aged 80–84 years: OR 0.55, $P=0.002$; aged ≥ 85 years: OR 0.42, $P=0.006$).

Risk scores such as the EuroSCORE are important decision criteria for SAVR or TF-TAVR. Among patients with low operative risk (EuroSCORE values <4), SAVR was the predominant treatment strategy, but risk-adjusted mortality did not differ significantly (OR 1.44, $P=0.308$). Patients at intermediate (EuroSCORE values ≥ 4 and ≤ 9) and high (EuroSCORE values >9) operative risk more frequently underwent TF-TAVR than SAVR. Whereas adjusted mortality in patients with intermediate risk was not significantly different (OR 0.81, $P=0.156$), patients at high operative risk benefit significantly from TF-TAVR (OR 0.62, $P=0.006$). Two

further subgroups showed decreased risk for in-hospital mortality after TF-TAVR compared with SAVR: symptomatic patients undergoing TF-TAVR in NYHA-Class III or IV had an odds ratio of 0.72 ($P=0.015$) for in-hospital death. Moreover, patients with advanced renal failure benefited from TF-TAVR after risk adjustment (OR 0.45, $P=0.005$). TF-TAVR was the most common treatment strategy in female patients and in patients suffering from peripheral artery disease, COPD, previous coronary artery bypass graft (CABG), pulmonary hypertension, and diabetes mellitus. In those subgroups, none of the treatment strategies showed significant advantages on in-hospital mortality (Figure 2).

Risk-Adjusted Complications in Different Subgroups

The treatment-related risk for in-hospital complications varied between the different subgroups and complications: The risk for stroke was not significantly different after risk-adjustment apart from patients with previous CABG, where the risk of stroke was smaller in patients undergoing TF-TAVR. The odds ratio for bleeding and prolonged ventilation was lower in patients undergoing TF-TAVR, the odds ratio for permanent pacemaker higher (Figure S1). In addition, TF-TAVR was associated with a shorter length of hospital stay than SAVR in all subgroups observed with most pronounced differences among patients aged ≥ 85 (–2.83 days, $P<0.001$), at high operative risk (–2.34 days, $P<0.001$), with previous CABG (–4.28 days, $P<0.001$), or with renal failure (–5.40 days, $P<0.001$, Figure S2).

Discussion

In this retrospective nationwide analysis of all patients treated with isolated surgical or transcatheter aortic valve replacement in 2014 and 2015 we found reduced in-hospital mortality after TF-TAVR in patients at high operative risk, aged >80 years, with advanced renal failure, and in patients suffering from severe dyspnea.

Over the analyzed time, TF-TAVR outnumbered SAVR procedures. In accordance with current guidelines, patients undergoing TF-TAVR had more co-morbidities and consequently an increased operative risk. This underlines that TF-TAVR evolved into the main treatment strategy for inoperable patients with severe aortic valve stenosis in clinical practice. Despite the advanced age and increased operative risk of patients undergoing TF-TAVR, the outcomes are comparable between both treatment strategies: in-hospital mortality, stroke rates, and permanent pacemaker implantations were higher, whereas need for transfusion of >5 red blood cell units or prolonged ventilation was lower after TF-TAVR. After adjustment for risk, the advantage of SAVR about in-hospital stroke and mortality disappeared, and risk for bleeding,

Table 3. In-Hospital Outcomes in Different Subgroups

	n	Age, Mean (y)	EuroSCORE, Mean	In-Hospital Mortality, %	Stroke, %	Acute Kidney Injury, %	Bleeding >5 Units, %	Mechanical Ventilation >48 H, %	New Permanent Pacemaker, %	Length of Hospital Stay, Mean D
Patients aged <75 y										
SAVR	8793	63.7	3.8	1.5%	1.4%	4.0%	7.8%	6.1%	4.0%	14.3
TF-TAVR	2280	69.7	8.3	2.5%	2.0%	6.1%	4.1%	4.4%	15.8%	15.3
Patients aged 75 to 79 y										
SAVR	3225	76.9	7.5	2.4%	2.1%	5.6%	11.5%	8.4%	3.9%	15.3
TF-TAVR	5067	77.3	11.0	2.5%	2.1%	5.5%	2.9%	2.8%	16.1%	14.7
Patients aged 80 to 84 y										
SAVR	980	81.5	9.8	4.1%	1.6%	8.7%	15.4%	8.7%	4.5%	15.9
TF-TAVR	7303	82.0	13.7	3.1%	2.6%	5.0%	3.3%	2.8%	17.1%	14.6
Patients aged ≥85 y										
SAVR	153	86.2	14.6	8.5%	XXX	12.4%	22.9%	16.3%	5.2%	18.4
TF-TAVR	5988	87.6	18.8	4.2%	XXX	6.0%	3.2%	2.6%	17.8%	15.4
Patients with EuroSCORE <4										
SAVR	6325	61.8	2.4	0.9%	0.7%	2.8%	5.6%	4.3%	3.7%	13.1
TF-TAVR	748	68.3	3.1	1.7%	0.5%	3.3%	2.0%	2.8%	15.2%	12.7
Patients with EuroSCORE 4 to 9										
SAVR	5056	74.2	5.8	2.3%	1.7%	5.3%	10.3%	7.3%	3.8%	15.2
TF-TAVR	7258	79.1	6.6	2.1%	1.3%	3.6%	2.3%	2.2%	15.3%	13.1
Patients with EuroSCORE >9										
SAVR	1770	76.4	14.4	5.1%	4.6%	10.8%	20.7%	15.8%	5.6%	19.4
TF-TAVR	12 632	83.0	18.8	4.0%	3.2%	6.8%	3.9%	3.3%	17.9%	16.1
Patients with female sex										
SAVR	5057	70.3	6.4	1.8%	1.5%	4.4%	10.4%	6.5%	3.8%	14.9
TF-TAVR	11 251	81.9	15.2	3.3%	2.5%	5.0%	3.6%	2.4%	16.4%	15.3
Patients with heart failure (NYHA III/IV)										
SAVR	3746	69.6	6.4	3.9%	1.8%	9.0%	12.7%	10.5%	4.5%	16.5
TF-TAVR	9572	81.2	15.4	4.3%	2.6%	8.1%	4.1%	4.2%	17.8%	16.4
Patients with previous CABG										
SAVR	248	69.7	12.4	2.8%	5.2%	6.9%	22.2%	13.7%	6.9%	18.0
TF-TAVR	1895	79.3	23.5	3.2%	2.3%	7.0%	3.4%	3.0%	16.8%	14.9
Patients with peripheral vascular disease										
SAVR	598	71.3	11.1	3.2%	2.3%	9.7%	14.2%	10.9%	4.0%	17.6
TF-TAVR	1835	80.7	23.5	4.1%	3.7%	8.4%	5.9%	4.9%	17.4%	16.8
Patients with COPD										
SAVR	1189	69.6	8.8	3.5%	1.6%	7.7%	13.8%	13.0%	4.0%	17.2
TF-TAVR	2711	80.1	19.2	4.2%	2.2%	8.0%	3.8%	4.7%	16.5%	16.5
Patients with pulmonary hypertension										
SAVR	1330	69.9	11.1	4.2%	2.0%	9.5%	15.2%	13.8%	5.2%	17.8
TF-TAVR	4286	81.3	23.1	4.6%	2.8%	7.9%	4.0%	3.7%	19.3%	17.0

Continued

Table 3. Continued

	n	Age, Mean (y)	EuroSCORE, Mean	In-Hospital Mortality, %	Stroke, %	Acute Kidney Injury, %	Bleeding >5 Units, %	Mechanical Ventilation >48 H, %	New Permanent Pacemaker, %	Length of Hospital Stay, Mean D
Patients with renal failure (GFR <30)										
SAVR	285	69.2	11.6	9.8%	4.2%	17.2%	38.9%	25.3%	6.7%	24.0
TF-TAVR	1362	80.3	23.7	7.0%	2.7%	12.6%	7.9%	6.2%	19.1%	19.1
Patients with diabetes mellitus										
SAVR	3311	70.3	6.0	2.5%	2.1%	7.5%	11.3%	10.1%	3.9%	16.0
TF-TAVR	6735	80.0	14.2	3.1%	2.6%	6.7%	3.4%	3.5%	17.7%	15.7

CABG indicates coronary artery bypass graft; COPD, chronic obstructive pulmonary disease; EuroSCORE, European System for Cardiac Operative Risk Evaluation; GFR, glomerular filtration rate; NYHA, New York Heart Association; SAVR, surgical aortic valve replacement; TF-TAVR, transfemoral transcatheter aortic valve replacement.

XXX: the value is not available anonymization concerns by the federal bureau of statistics.

prolonged ventilation, and acute kidney failure was higher after SAVR. This confirms that results after TF-TAVR further improved even in real-world clinical practice because of technical improvements and learning curves.⁶ Therefore, TF-TAVR is now a reasonable alternative to the established SAVR.¹⁷ Nevertheless, different pathologies in younger patients, the need for permanent pacemaker implantations, and uncertain durability raises concerns over the increase of TF-TAVR indications, although intermediate-term data have not revealed differences between SAVR and TAVR.^{18–21} It is therefore crucial to identify the patient subgroups which benefit most from SAVR or TF-TAVR. Several studies have compared the outcomes after SAVR and TAVR, but subgroup analyses are rare.^{9,22–24} This may be because of limited cohort sizes in studies and resulting difficulties in getting statistically significant results for subgroups. In recent randomized controlled trials comparing TAVR and SAVR multiple subgroup analyses were performed, but received wide confidence intervals and therefore many results did not achieve statistical significance.^{3,25} A recently published propensity matched analysis including 9000 patients undergoing SAVR or transapical and transfemoral TAVR in the United States did not find significant differences in 1-year mortality even in distinct subgroups.²⁶ Therefore, we performed risk-adjusted analyses in different subgroups of a large real-world cohort.¹⁴ Subgroups in the present retrospective study were pre-defined by typical risk factors for in-hospital complications such as age, EuroSCORE, sex category, advanced heart failure, peripheral vascular disease, COPD, previous CABG, pulmonary hypertension, renal failure, and diabetes mellitus.^{27–30} Within those subgroups, we found mixed results on in-hospital outcomes. Risk of stroke was similar apart from patients with previous CABG undergoing TF-TAVR. They had a reduced risk for stroke after risk adjustment. This is in line with previous studies, which

identified previous CABG as a risk factor for stroke after SAVR.^{29,31} According to randomized controlled trials, acute kidney injuries and relevant bleeding occurred more frequently in patients undergoing SAVR after risk adjustment.²⁴ Prolonged ventilation was less frequently necessary in patients undergoing TAVR, indicating that TF-TAVR develops towards a minimalist approach in all analyzed subgroups.³² Consequently, length of hospital stay was shorter after TF-TAVR after risk adjustment.

In contrast to the comparison of all patients undergoing SAVR or TF-TAVR, in-hospital mortality did differ within particular subgroups. The risk of mortality was lower in patients undergoing TF-TAVR and aged >80 years, and this finding was even more pronounced in patients aged >85 years. These data confirm, in accordance with other studies, that TF-TAVR is the superior treatment strategy for octogenarians with severe aortic valve stenosis.^{13,18}

TAVR was initially developed for patients with aortic valve stenosis at increased operative risk.³³ The present study shows that patients at increased operative risk, defined as a EuroSCORE >99, had decreased risk for mortality after TF-TAVR compared with SAVR in a real-world collective. Since a logistic EuroSCORE of 9 is equivalent to an STS score of 4,³⁴ our data are in line with propensity-matched comparison of TF-TAVR and SAVR in the PARTNER II trial, which found favorable outcomes of balloon-expandable TF-TAVR in patients at intermediate risk.¹² In contrast, patients treated with a self-expandable TF-TAVR had significantly reduced 2-year mortality, if the STS score was <7.³⁵ Two further subgroups benefit from TF-TAVR: as considered in the established risk scores for cardiac surgery, patients with severe dyspnea or with advanced renal failure are at increased risk for mortality. Accordingly, in-hospital mortality of patients in NYHA Class III/IV and advanced renal failure was significantly lower if they underwent TF-TAVR.

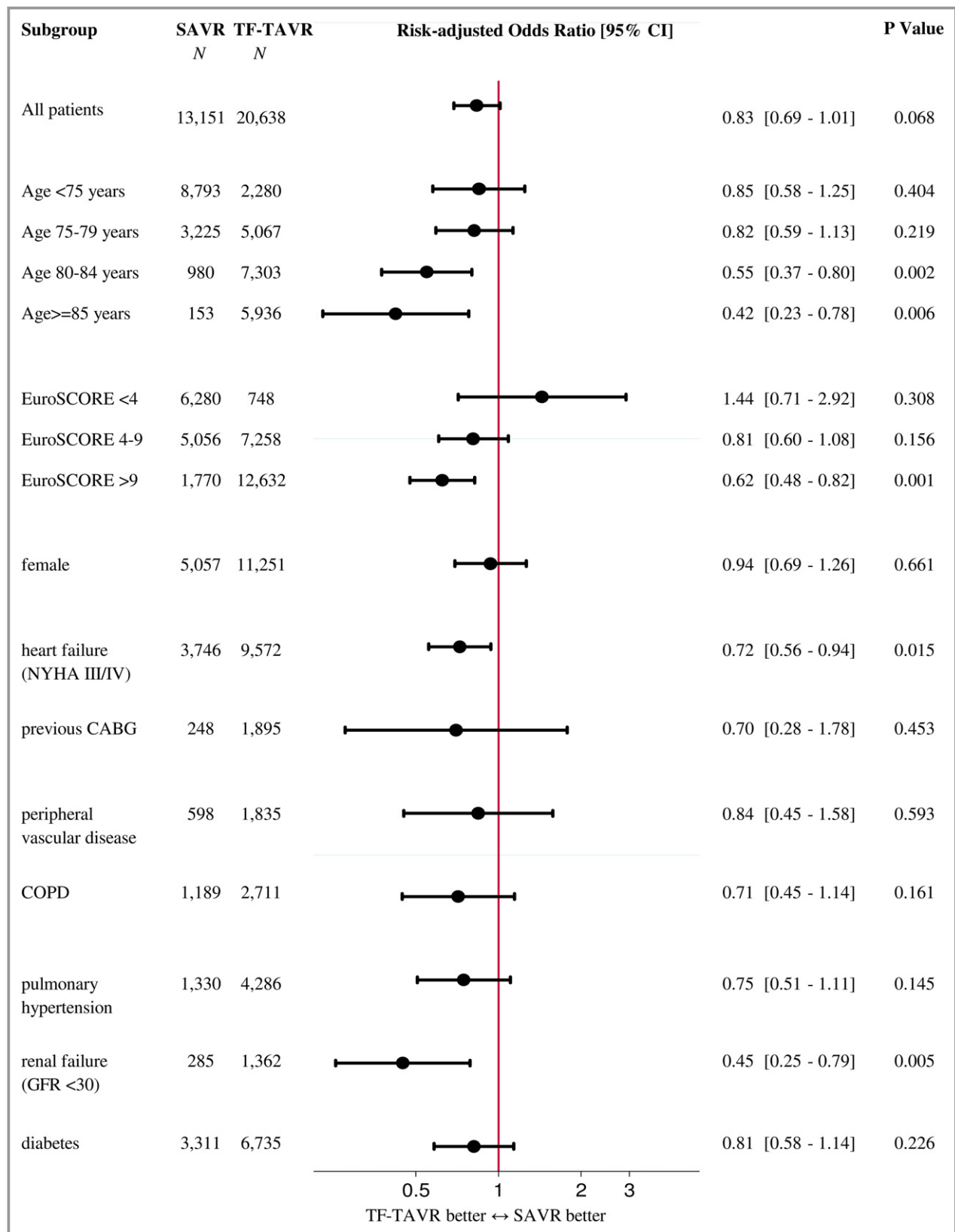


Figure 2. Subgroup-specific treatment effects on in-hospital mortality. Results of multivariate logistic regression analyses with 20 predefined baseline patient characteristics included as potential confounders (all covariates listed in Table 1). CABG indicates coronary artery bypass graft; COPD, chronic obstructive pulmonary disease; EuroSCORE, European System for Cardiac Operative Risk Evaluation; GFR, glomerular filtration rate; NYHA, New York Heart Association.

Limitations

First of all, the chosen comparison (SAVR versus TF-TAVR) assumes that the transfemoral approach is anatomically feasible. Furthermore, apart from the limitations typically associated with retrospective studies, the analysis has several specific limitations: It is based on administrative data, designed to report diagnoses and procedures, and intended to trigger reimbursement. Hence, while the competing interests of hospitals and sickness funds should ensure a high level of data reliability and quality, coding errors cannot be ruled out with certainty, in particular with codes that do not impact reimbursement (such as previous stroke, new atrioventricular block or left bundle branch block, anticoagulation therapy).

Moreover, the administrative data set lacks relevant clinical information (such as echocardiographic findings or anatomical characteristics), preventing operative risk assessment and a better understanding of the underlying valvular pathomechanism. Therefore, only an approximation of the logistic EuroSCORE, in fact a conservative or ‘best-case scenario’ estimate, is applied.

When estimating treatment effects, adjusted differences in in-hospital outcomes may be interpreted as procedure-related effects if all decision- and outcome-relevant-parameters are used for risk adjustment. Unfortunately, we cannot guarantee that all parameters of relevance are included in the model. Furthermore, even the decision-making process within the different centers may differ substantially: most centers might have implemented a transfemoral-first approach as part of the decision process within the interdisciplinary ‘Heart Team’, and some centers might not even have a ‘Heart Team’. In addition, long-term follow up data are missing, as DESTATIS provides no longitudinal data or cross-links with other clinical or administrative data sets. Finally, this analysis relies on data from the German healthcare system and other countries’ experiences may differ.

Conclusions

In this study evaluating clinical practice in Germany, we compare in-hospital outcomes of surgical (SAVR) and transfemoral transcatheter aortic valve replacement (TF-TAVR) procedures based on ICD and OPS codes to identify subgroups of patients for whom either SAVR or TF-TAVR would be superior. After risk-adjustment, data show that TF-TAVR is associated with a decreased risk for in-hospital mortality in patients with an age >80 years, at high operative risk, with advanced renal failure, and in NYHA Class III or IV. Outcomes for SAVR or TF-TAVR in the remaining subgroups were comparable.

Sources of Funding

The study was supported by internal funding of the University Heart Center Freiburg.

Disclosures

None.

References

- Cribier A, Eltchaninoff H, Bash A, Borenstein N, Tron C, Bauer F, Derumeaux G, Anselme F, Laborde F, Leon MB. Percutaneous transcatheter implantation of an aortic valve prosthesis for calcific aortic stenosis: first human case description. *Circulation*. 2002;106:3006–8.
- Leon MB, Smith CR, Mack M, Miller DC, Moses JW, Svensson LG, Tuzcu EM, Webb JG, Fontana GP, Makkar RR, Brown DL, Block PC, Guyton RA, Pichard AD, Bavaria JE, Herrmann HC, Douglas PS, Petersen JL, Akin JJ, Anderson WN, Wang D, Pocock S, PARTNER Trial Investigators. Transcatheter aortic-valve implantation for aortic stenosis in patients who cannot undergo surgery. *N Engl J Med*. 2010;363:1597–607.
- Adams DH, Popma JJ, Reardon MJ, Yakubov SJ, Coselli JS, Deeb GM, Gleason TG, Buchbinder M, Hermiller J Jr, Kleiman NS, Chetcuti S, Heiser J, Merhi W, Zorn G, Tadros P, Robinson N, Petrossian G, Hughes GC, Harrison JK, Conte J, Maini B, Mumtaz M, Chenoweth S, Oh JK, U.S. CoreValve Clinical Investigators. Transcatheter aortic-valve replacement with a self-expanding prosthesis. *N Engl J Med*. 2014;370:1790–8.
- Nishimura RA, Otto CM, Bonow RO, Carabello BA, Erwin JP III, Guyton RA, O’Gara PT, Ruiz CE, Skubas NJ, Sorajja P, Sundt TM III, Thomas JD, ACC/AHA Task Force Members. 2014 AHA/ACC Guideline for the Management of Patients With Valvular Heart Disease: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. *Circulation*. 2014;129:e521–643.
- Reinohl J, Kaier K, Reinecke H, Schmoor C, Frankenstein L, Vach W, Cribier A, Beyersdorf F, Bode C, Zehender M. Effect of availability of transcatheter aortic-valve replacement on clinical practice. *N Engl J Med*. 2015;373:2438–47.
- Kaier K, Reinecke H, Schmoor C, Frankenstein L, Vach W, Hehn P, Zirlirk A, Bode C, Zehender M, Reinohl J. Learning curves among all patients undergoing transcatheter aortic valve implantation in Germany: a retrospective observational study. *Int J Cardiol*. 2017;235:17–21.
- Walther T, Hamm CW, Schuler G, Berkowitsch A, Kottling J, Mangner N, Mudra H, Beckmann A, Cremer J, Welz A, Lange R, Kuck KH, Mohr FW, Mollmann H, Board GE. Perioperative results and complications in 15,964 transcatheter aortic valve replacements: prospective data from the GARY registry. *J Am Coll Cardiol*. 2015;65:2173–80.
- Gilard M, Eltchaninoff H, Donzeau-Gogue P, Chevrel K, Fajadet J, Leprince P, Leguerrier A, Lievre M, Prat A, Teiger E, Lefevre T, Tchetché D, Carrie D, Himbert D, Albat B, Cribier A, Sudre A, Blanchard D, Rioufol G, Collet F, Houel R, Dos Santos P, Meneveau N, Ghostine S, Manigold T, Guyon P, Grisoli D, Le Breton H, Delpine S, Didier R, Favereau X, Souteyrand G, Ohlmann P, Doisy V, Grollier G, Gommeaux A, Claudel JP, Bourlon F, Bertrand B, Laskar M, lung B, FRANCE 2 Investigators. Late outcomes of transcatheter aortic valve replacement in high-risk patients: the FRANCE-2 registry. *J Am Coll Cardiol*. 2016;68:1637–1647.
- Nguyen V, Michel M, Eltchaninoff H, Gilard M, Dindorf C, lung B, Mossialos E, Cribier A, Vahanian A, Chevrel K, Messika-Zeitoun D. Implementation of transcatheter aortic valve replacement in France. *J Am Coll Cardiol*. 2018;71:1614–1627.
- Reardon MJ, Van Mieghem NM, Popma JJ, Kleiman NS, Sondergaard L, Mumtaz M, Adams DH, Deeb GM, Maini B, Gada H, Chetcuti S, Gleason T, Heiser J, Lange R, Merhi W, Oh JK, Olsen PS, Piazza N, Williams M, Windecker S, Yakubov SJ, Grube E, Makkar R, Lee JS, Conte J, Vang E, Nguyen H, Chang Y, Mugglin AS, Serruys PW, Kappetein AP; SURTAVI Investigators. Surgical or transcatheter aortic-valve replacement in intermediate-risk patients. *N Engl J Med*. 2017;376:1321–1331.
- Leon MB, Smith CR, Mack MJ, Makkar RR, Svensson LG, Kodali SK, Thourani VH, Tuzcu EM, Miller DC, Herrmann HC, Doshi D, Cohen DJ, Pichard AD, Kapadia S, Dewey T, Babaliaros V, Szeto WY, Williams MR, Kereiakes D, Zajarias A, Greason KL, Whisenant BK, Hodson RW, Moses JW, Trento A, Brown DL, Fearon WF, Pibarot P, Hahn RT, Jaber WA, Anderson WN, Alu MC, Webb JG, PARTNER 2 Investigators. Transcatheter or surgical aortic-valve replacement in intermediate-risk patients. *N Engl J Med*. 2016;374:1609–20.

12. Thourani VH, Kodali S, Makkar RR, Herrmann HC, Williams M, Babaliaros V, Smalling R, Lim S, Malaisrie SC, Kapadia S, Szeto WY, Greason KL, Kereiakes D, Ailawadi G, Whisenant BK, Devireddy C, Leipsic J, Hahn RT, Pibarot P, Weissman NJ, Jaber WA, Cohen DJ, Suri R, Tuzcu EM, Svensson LG, Webb JG, Moses JW, Mack MJ, Miller DC, Smith CR, Alu MC, Parvataneni R, D'Agostino RB Jr, Leon MB. Transcatheter aortic valve replacement versus surgical valve replacement in intermediate-risk patients: a propensity score analysis. *Lancet*. 2016;387:2218–25.
13. Baumgartner H, Falk V, Bax JJ, De Bonis M, Hamm C, Holm PJ, Jung B, Lancellotti P, Lansac E, Rodriguez Munoz D, Rosenhek R, Sjogren J, Tornos Mas P, Vahanian A, Walther T, Wendler O, Windecker S, Zamorano JL; ESC Scientific Document Group. 2017 ESC/EACTS Guidelines for the management of valvular heart disease. *Eur Heart J*. 2017;38:2739–2791.
14. Elze MC, Gregson J, Baber U, Williamson E, Sartori S, Mehran R, Nichols M, Stone GW, Pocock SJ. Comparison of propensity score methods and covariate adjustment: evaluation in 4 cardiovascular studies. *J Am Coll Cardiol*. 2017;69:345–357.
15. Braitman LE, Rosenbaum PR. Rare outcomes, common treatments: analytic strategies using propensity scores. *Ann Intern Med*. 2002;137:693–5.
16. Vansteelandt S, Daniel RM. On regression adjustment for the propensity score. *Stat Med*. 2014;33:4053–72.
17. Sondergaard L. Time to explore transcatheter aortic valve replacement in younger. Low-Risk Patients. *JACC Cardiovasc Interv*. 2016;9:2183–2185.
18. Mack MJ, Leon MB, Smith CR, Miller DC, Moses JW, Tuzcu EM, Webb JG, Douglas PS, Anderson WN, Blackstone EH, Kodali SK, Makkar RR, Fontana GP, Kapadia S, Bavaria J, Hahn RT, Thourani VH, Babaliaros V, Pichard A, Herrmann HC, Brown DL, Williams M, Akin J, Davidson MJ, Svensson LG; investigators Pt. 5-year outcomes of transcatheter aortic valve replacement or surgical aortic valve replacement for high surgical risk patients with aortic stenosis (PARTNER 1): a randomised controlled trial. *Lancet*. 2015;385:2477–84.
19. Deeb GM, Reardon MJ, Chetcuti S, Patel HJ, Grossman PM, Yakubov SJ, Kleiman NS, Coselli JS, Gleason TG, Lee JS, Hermiller JB Jr, Heiser J, Merhi W, Zorn GL III, Tadros P, Robinson N, Petrossian G, Hughes GC, Harrison JK, Maini B, Mumtaz M, Conte J, Resar J, Aharonian V, Pfeffer T, Oh JK, Qiao H, Adams DH, Popma JJ, CoreValve US Clinical Investigators. 3-Year outcomes in high-risk patients who underwent surgical or transcatheter aortic valve replacement. *J Am Coll Cardiol*. 2016;67:2565–74.
20. Subramanian R, Olson LJ, Edwards WD. Surgical pathology of pure aortic stenosis: a study of 374 cases. *Mayo Clin Proc*. 1984;59:683–90.
21. Stachon P, Kaier K, Zirlik A, Reinohl J, Heidt T, Bothe W, Hehn P, Zehender M, Bode C, von Zur Muhlen C. Risk factors and outcome of postoperative delirium after transcatheter aortic valve replacement. *Clin Res Cardiol*. 2018;107:756–762.
22. Stachon P, Zehender M, Bode C, von Zur Muhlen C, Kaier K. Development and in-hospital mortality of transcatheter and surgical aortic valve replacement in 2015 in Germany. *J Am Coll Cardiol*. 2018;72:475–476.
23. Piazza N, Kalesan B, van Mieghem N, Head S, Wenaweser P, Carrel TP, Bleiziffer S, de Jaegere PP, Gahl B, Anderson RH, Kappetein AP, Lange R, Serruys PW, Windecker S, Juni P. A 3-center comparison of 1-year mortality outcomes between transcatheter aortic valve implantation and surgical aortic valve replacement on the basis of propensity score matching among intermediate-risk surgical patients. *JACC Cardiovasc Interv*. 2013;6:443–51.
24. Siontis GC, Praz F, Pilgrim T, Mavridis D, Verma S, Salanti G, Sondergaard L, Juni P, Windecker S. Transcatheter aortic valve implantation vs. surgical aortic valve replacement for treatment of severe aortic stenosis: a meta-analysis of randomized trials. *Eur Heart J*. 2016;37:3503–3512.
25. Sondergaard L, Steinbruechel DA, Ihlemann N, Nissen H, Kjeldsen BJ, Petursson P, Ngo AT, Olsen NT, Chang Y, Franzen OW, Engstrom T, Clemmensen P, Olsen PS, Thyregod HG. Two-year outcomes in patients with severe aortic valve stenosis randomized to transcatheter versus surgical aortic valve replacement: the all-comers nordic aortic valve intervention randomized clinical trial. *Circ Cardiovasc Interv*. 2016;9:e003665.
26. Brennan JM, Thomas L, Cohen DJ, Shahian D, Wang A, Mack MJ, Holmes DR, Edwards FH, Frankel NZ, Baron SJ, Carroll J, Thourani V, Tuzcu EM, Arnold SV, Cohn R, Maser T, Schawe B, Strong S, Stickfort A, Patrick-Lake E, Graham FL, Dai D, Li F, Matsouaka RA, O'Brien S, Li F, Pencina MJ, Peterson ED. Transcatheter versus surgical aortic valve replacement: propensity-matched comparison. *J Am Coll Cardiol*. 2017;70:439–450.
27. Roques F, Michel P, Goldstone AR, Nashef SA. The logistic EuroSCORE. *Eur Heart J*. 2003;24:881–2.
28. O'Brien SM, Shahian DM, Filardo G, Ferraris VA, Haan CK, Rich JB, Normand SL, DeLong ER, Shewan CM, Dokholyan RS, Peterson ED, Edwards FH, Anderson RP; Society of Thoracic Surgeons Quality Measurement Task Force. The Society of Thoracic Surgeons 2008 cardiac surgery risk models: part 2— isolated valve surgery. *Ann Thorac Surg*. 2009;88:S23–42.
29. Reinohl J, Psyrrakis D, Kaier K, Kodirov S, Siepe M, Gutmann A, von Zur Muhlen C, Moser M, Ahrens I, Pache G, Zirlik A, Langer M, Beyersdorf F, Zehender M, Bode C, Blanke P. Aortic root volume is associated with contained rupture of the aortic annulus in balloon-expandable transcatheter aortic valve replacement. *Catheter Cardiovasc Interv*. 2016;87:807–17.
30. Gutmann A, Kaier K, Reinecke H, Frankestein L, Zirlik A, Bothe W, von Zur Muhlen C, Zehender M, Reinohl J, Bode C, Stachon P. Impact of pulmonary hypertension on in-hospital outcome after surgical or transcatheter aortic valve replacement. *EuroIntervention*. 2017;13:804–810.
31. Castellat P, Didier R, Bezon E, Couturaud F, Eltchaninoff H, Jung B, Donzeau-Gouge P, Chevreul K, Fajadet J, Leprince P, Leguerrier A, Lieve M, Prat A, Teiger E, Laskar M, Boschat J, Gilard M; FRANCE 2 Investigators. Comparison of outcome of transcatheter aortic valve implantation with versus without previous coronary artery bypass grafting (from the FRANCE 2 Registry). *Am J Cardiol*. 2015;116:420–5.
32. Hosoba S, Yamamoto M, Shioda K, Sago M, Koyama Y, Shimura T, Kagase A, Tada N, Naganuma T, Araki M, Yamanaka F, Shirai S, Watanabe Y, Hayashida K. Safety and efficacy of minimalist approach in transfemoral transcatheter aortic valve replacement: insights from the Optimized transCathEter vAlvular interventioN-Transcatheter Aortic Valve Implantation (OCEAN-TAVI) registry. *Interact Cardiovasc Thorac Surg*. 2018;26:420–424.
33. Cribier A, Eltchaninoff H, Tron C, Bauer F, Agatiello C, Sebah L, Bash A, Nusimovici D, Litzler PY, Bessou JP, Leon MB. Early experience with percutaneous transcatheter implantation of heart valve prosthesis for the treatment of end-stage inoperable patients with calcific aortic stenosis. *J Am Coll Cardiol*. 2004;43:698–703.
34. Piazza N, Wenaweser P, van Gameren M, Pilgrim T, Zikas A, Otten A, Nuis R, Onuma Y, Cheng JM, Kappetein AP, Boersma E, Juni P, de Jaegere P, Windecker S, Serruys PW. Relationship between the logistic EuroSCORE and the Society of Thoracic Surgeons Predicted Risk of Mortality score in patients implanted with the CoreValve ReValving system—a Bern-Rotterdam Study. *Am Heart J*. 2010;159:323–9.
35. Reardon MJ, Adams DH, Kleiman NS, Yakubov SJ, Coselli JS, Deeb GM, Gleason TG, Lee JS, Hermiller JB Jr, Chetcuti S, Heiser J, Merhi W, Zorn GL III, Tadros P, Robinson N, Petrossian G, Hughes GC, Harrison JK, Maini B, Mumtaz M, Conte JV, Resar JR, Aharonian V, Pfeffer T, Oh JK, Qiao H, Popma JJ. 2-Year outcomes in patients undergoing surgical or self-expanding transcatheter aortic valve replacement. *J Am Coll Cardiol*. 2015;66:113–21.

SUPPLEMENTAL MATERIAL

Table S1. Diagnosis and procedure codes used for this analysis.

OPS codes

5-351.0*	Surgical aortic valve replacement
5-35a.0*	Transcatheter aortic valve replacement
5-361.*, 5-362.*, 5-363.*,	Coronary artery bypass graft
5-351.1*, 5-351.2*, 5-353.1, 5-353.2	Surgical mitral valve replacement/reconstruction
5-351.4*	Surgical tricuspid valve replacement
5-377.0 et seqq.	Permanent pacemaker implantation

8-800.7* Transfusion of RBC
 since 2010:
 8-800.c*

Diagnosis

I35.0, I06.0	Aortic valve stenosis (degenerative/rheumatic)
I35.2, I06.2	Combined aortic valve diseases (degenerative/rheumatic)
I50.1*	Left ventricular congestive heart failure (<i>according to NYHA classes</i>)
I10*	Arterial Hypertension
I25.11, I25.12, I25.13	Coronary artery disease
I25.20, I25.21, I25.22	Previous myocardial infarction (<i>within 4 months/1 year/after 1 year</i>)
Z95.1	Previous coronary artery bypass graft
Z95.1 – Z95.4	Previous cardiac surgery
I70.20-I70.25, I70.8, I70.9, I73.9	Peripheral vascular disease
I65.2	Carotid disease
I21*	Acute myocardial infarction (<i>within the last 28 days</i>)
J44*	Chronic obstructive pulmonary disease
I27*	Pulmonary hypertension
N18*	Renal disease
N17*	Acute kidney injury
I48.1*	Atrial fibrillation
E10* - E14*	Diabetes
I63*, I64	Stroke or cerebral infarction incl. occlusion and stenosis of cerebral and precerebral arteries, resulting in cerebral infarction

Tables S2-S17 Legends (see Excel file):

Table S2. Analysis details, all patients (N=33,789).

Analysis strategy 1: Covariate adjustment: Logistic regression models with a random intercept at the center level

Analysis strategy 2: Propensity score adjustment: First, a logistic regression model was performed on all patient and procedural characteristics to calculate the propensity score. The propensity score represents the likelihood that the patient was in the TF-TAVR arm. Then, logistic regression models with a random intercept at the center level, the propensity score as continuous covariate and year 2015 as additional confounder were conducted.

SAVR: surgical aortic valve replacement; TF-TAVR: transfemoral transcatheter aortic valve replacement; SD: standard deviation; CAD: coronary artery disease; MI: myocardial infarction; CABG: coronary artery bypass graft; COPD: chronic obstructive pulmonary disease; GFR: glomerular filtration rate.

Table S3. Analysis details, patients <75 years of age (N= 11,073).

Analysis strategy 1: Covariate adjustment: Logistic regression models with a random intercept at the center level

Analysis strategy 2: Propensity score adjustment: First, a logistic regression model was performed on all patient and procedural characteristics to calculate the propensity score. The propensity score represents the likelihood that the patient was in the TF-TAVR arm. Then, logistic regression models with a random intercept at the center level, the propensity score as continuous covariate and year 2015 as additional confounder were conducted.

SAVR: surgical aortic valve replacement; TF-TAVR: transfemoral transcatheter aortic valve replacement; SD: standard deviation; CAD: coronary artery disease; MI: myocardial infarction; CABG: coronary artery bypass graft; COPD: chronic obstructive pulmonary disease; GFR: glomerular filtration rate.

Table S4. Analysis details, patients <80 years of age (N=8,292).

Analysis strategy 1: Covariate adjustment: Logistic regression models with a random intercept at the center level

Analysis strategy 2: Propensity score adjustment: First, a logistic regression model was performed on all patient and procedural characteristics to calculate the propensity score. The propensity score represents the likelihood that the patient was in the TF-TAVR arm. Then, logistic regression models with a random intercept at the center level, the propensity score as continuous covariate and year 2015 as additional confounder were conducted.

SAVR: surgical aortic valve replacement; TF-TAVR: transfemoral transcatheter aortic valve replacement; SD: standard deviation; CAD: coronary artery disease; MI: myocardial infarction; CABG: coronary artery bypass graft; COPD: chronic obstructive pulmonary disease; GFR: glomerular filtration rate.

Table S5. Analysis details, patients <85 years of age (N=8,283).

Analysis strategy 1: Covariate adjustment: Logistic regression models with a random intercept at the center level

Analysis strategy 2: Propensity score adjustment: First, a logistic regression model was performed on all patient and procedural characteristics to calculate the propensity score. The propensity score represents the likelihood that the patient was in the TF-TAVR arm. Then, logistic regression models with a random intercept at the center level, the propensity score as continuous covariate and year 2015 as additional confounder were conducted.

SAVR: surgical aortic valve replacement; TF-TAVR: transfemoral transcatheter aortic valve replacement; SD: standard deviation; CAD: coronary artery disease; MI: myocardial infarction; CABG: coronary artery bypass graft; COPD: chronic obstructive pulmonary disease; GFR: glomerular filtration rate.

Table S6. Analysis details, patients 85+ years of age (N= 6,141).

Analysis strategy 1: Covariate adjustment: Logistic regression models with a random intercept at the center level

Analysis strategy 2: Propensity score adjustment: First, a logistic regression model was performed on all patient and procedural characteristics to calculate the propensity score. The propensity score represents the likelihood that the patient was in the TF-TAVR arm. Then, logistic regression models with a random intercept at the center level, the propensity score as continuous covariate and year 2015 as additional confounder were conducted.

SAVR: surgical aortic valve replacement; TF-TAVR: transfemoral transcatheter aortic valve replacement; SD: standard deviation; CAD: coronary artery disease; MI: myocardial infarction; CABG: coronary artery bypass graft; COPD: chronic obstructive pulmonary disease; GFR: glomerular filtration rate.

Table S7. Analysis details, female patients (N=16,308).

Analysis strategy 1: Covariate adjustment: Logistic regression models with a random intercept at the center level

Analysis strategy 2: Propensity score adjustment: First, a logistic regression model was performed on all patient and procedural characteristics to calculate the propensity score. The propensity score represents the likelihood that the patient was in the TF-TAVR arm. Then, logistic regression models with a random intercept at the center level, the propensity score as continuous covariate and year 2015 as additional confounder were conducted.

SAVR: surgical aortic valve replacement; TF-TAVR: transfemoral transcatheter aortic valve replacement; SD: standard deviation; CAD: coronary artery disease; MI: myocardial infarction; CABG: coronary artery bypass graft; COPD: chronic obstructive pulmonary disease; GFR: glomerular filtration rate.

Table S8. Analysis details, patients in NYHA class III or IV (N=13,318).

Analysis strategy 1: Covariate adjustment: Logistic regression models with a random intercept at the center level

Analysis strategy 2: Propensity score adjustment: First, a logistic regression model was performed on all patient and procedural characteristics to calculate the propensity score. The propensity score represents the likelihood that the patient was in the TF-TAVR arm. Then, logistic regression models with a random intercept at the center level, the propensity score as continuous covariate and year 2015 as additional confounder were conducted.

SAVR: surgical aortic valve replacement; TF-TAVR: transfemoral transcatheter aortic valve replacement; SD: standard deviation; CAD: coronary artery disease; MI: myocardial infarction; CABG: coronary artery bypass graft; COPD: chronic obstructive pulmonary disease; GFR: glomerular filtration rate.

Table S9. Analysis details, patients with previous CABG (N=2,143).

Analysis strategy 1: Covariate adjustment: Logistic regression models with a random intercept at the center level

Analysis strategy 2: Propensity score adjustment: First, a logistic regression model was performed on all patient and procedural characteristics to calculate the propensity score. The propensity score represents the likelihood that the patient was in the TF-TAVR arm. Then, logistic regression models with a random intercept at the center level, the propensity score as continuous covariate and year 2015 as additional confounder were conducted.

SAVR: surgical aortic valve replacement; TF-TAVR: transfemoral transcatheter aortic valve replacement; SD: standard deviation; CAD: coronary artery disease; MI: myocardial infarction; CABG: coronary artery bypass graft; COPD: chronic obstructive pulmonary disease; GFR: glomerular filtration rate.

Table S10. Analysis details, patients with atherosclerotic disease (N=2,433).

Analysis strategy 1: Covariate adjustment: Logistic regression models with a random intercept at the center level

Analysis strategy 2: Propensity score adjustment: First, a logistic regression model was performed on all patient and procedural characteristics to calculate the propensity score. The propensity score represents the likelihood that the patient was in the TF-TAVR arm. Then, logistic regression models with a random intercept at the center level, the propensity score as continuous covariate and year 2015 as additional confounder were conducted.

SAVR: surgical aortic valve replacement; TF-TAVR: transfemoral transcatheter aortic valve replacement; SD: standard deviation; CAD: coronary artery disease; MI: myocardial infarction; CABG: coronary artery bypass graft; COPD: chronic obstructive pulmonary disease; GFR: glomerular filtration rate.

Table S11. Analysis details, patients with COPD (N=3,900).

Analysis strategy 1: Covariate adjustment: Logistic regression models with a random intercept at the center level

Analysis strategy 2: Propensity score adjustment: First, a logistic regression model was performed on all patient and procedural characteristics to calculate the propensity score. The propensity score represents the likelihood that the patient was in the TF-TAVR arm. Then, logistic regression models with a random intercept at the center level, the propensity score as continuous covariate and year 2015 as additional confounder were conducted.

SAVR: surgical aortic valve replacement; TF-TAVR: transfemoral transcatheter aortic valve replacement; SD: standard deviation; CAD: coronary artery disease; MI: myocardial infarction; CABG: coronary artery bypass graft; COPD: chronic obstructive pulmonary disease; GFR: glomerular filtration rate.

Table S12. Analysis details, patients with pulmonary hypertension (N=5,616).

Analysis strategy 1: Covariate adjustment: Logistic regression models with a random intercept at the center level

Analysis strategy 2: Propensity score adjustment: First, a logistic regression model was performed on all patient and procedural characteristics to calculate the propensity score. The propensity score represents the likelihood that the patient was in the TF-TAVR arm. Then, logistic regression models with a random intercept at the center level, the propensity score as continuous covariate and year 2015 as additional confounder were conducted.

SAVR: surgical aortic valve replacement; TF-TAVR: transfemoral transcatheter aortic valve replacement; SD: standard deviation; CAD: coronary artery disease; MI: myocardial infarction; CABG: coronary artery bypass graft; COPD: chronic obstructive pulmonary disease; GFR: glomerular filtration rate.

Table S13. Analysis details, patients with GFR < 30ml (N=1,647).

Analysis strategy 1: Covariate adjustment: Logistic regression models with a random intercept at the center level

Analysis strategy 2: Propensity score adjustment: First, a logistic regression model was performed on all patient and procedural characteristics to calculate the propensity score. The propensity score represents the likelihood that the patient was in the TF-TAVR arm. Then, logistic regression models with a random intercept at the center level, the propensity score as continuous covariate and year 2015 as additional confounder were conducted.

SAVR: surgical aortic valve replacement; TF-TAVR: transfemoral transcatheter aortic valve replacement; SD: standard deviation; CAD: coronary artery disease; MI: myocardial infarction; CABG: coronary artery bypass graft; COPD: chronic obstructive pulmonary disease; GFR: glomerular filtration rate.

Table S14. Analysis details, patients with diabetes (N=10,046).

Analysis strategy 1: Covariate adjustment: Logistic regression models with a random intercept at the center level

Analysis strategy 2: Propensity score adjustment: First, a logistic regression model was performed on all patient and procedural characteristics to calculate the propensity score. The propensity score

represents the likelihood that the patient was in the TF-TAVR arm. Then, logistic regression models with a random intercept at the center level, the propensity score as continuous covariate and year 2015 as additional confounder were conducted.

SAVR: surgical aortic valve replacement; TF-TAVR: transfemoral transcatheter aortic valve replacement; SD: standard deviation; CAD: coronary artery disease; MI: myocardial infarction; CABG: coronary artery bypass graft; COPD: chronic obstructive pulmonary disease; GFR: glomerular filtration rate.

Table S15. Analysis details, patients with EuroSCORE < 4 (N=7,053).

Analysis strategy 1: Covariate adjustment: Logistic regression models with a random intercept at the center level

Analysis strategy 2: Propensity score adjustment: First, a logistic regression model was performed on all patient and procedural characteristics to calculate the propensity score. The propensity score represents the likelihood that the patient was in the TF-TAVR arm. Then, logistic regression models with a random intercept at the center level, the propensity score as continuous covariate and year 2015 as additional confounder were conducted.

SAVR: surgical aortic valve replacement; TF-TAVR: transfemoral transcatheter aortic valve replacement; SD: standard deviation; CAD: coronary artery disease; MI: myocardial infarction; CABG: coronary artery bypass graft; COPD: chronic obstructive pulmonary disease; GFR: glomerular filtration rate.

Table S16. Analysis details, patients with EuroSCORE 4-9 (N=12,314).

Analysis strategy 1: Covariate adjustment: Logistic regression models with a random intercept at the center level

Analysis strategy 2: Propensity score adjustment: First, a logistic regression model was performed on all patient and procedural characteristics to calculate the propensity score. The propensity score represents the likelihood that the patient was in the TF-TAVR arm. Then, logistic regression models with a random intercept at the center level, the propensity score as continuous covariate and year 2015 as additional confounder were conducted.

SAVR: surgical aortic valve replacement; TF-TAVR: transfemoral transcatheter aortic valve replacement; SD: standard deviation; CAD: coronary artery disease; MI: myocardial infarction; CABG: coronary artery bypass graft; COPD: chronic obstructive pulmonary disease; GFR: glomerular filtration rate.

Table S17. Analysis details, patients with EuroSCORE >9 (N=14,402).

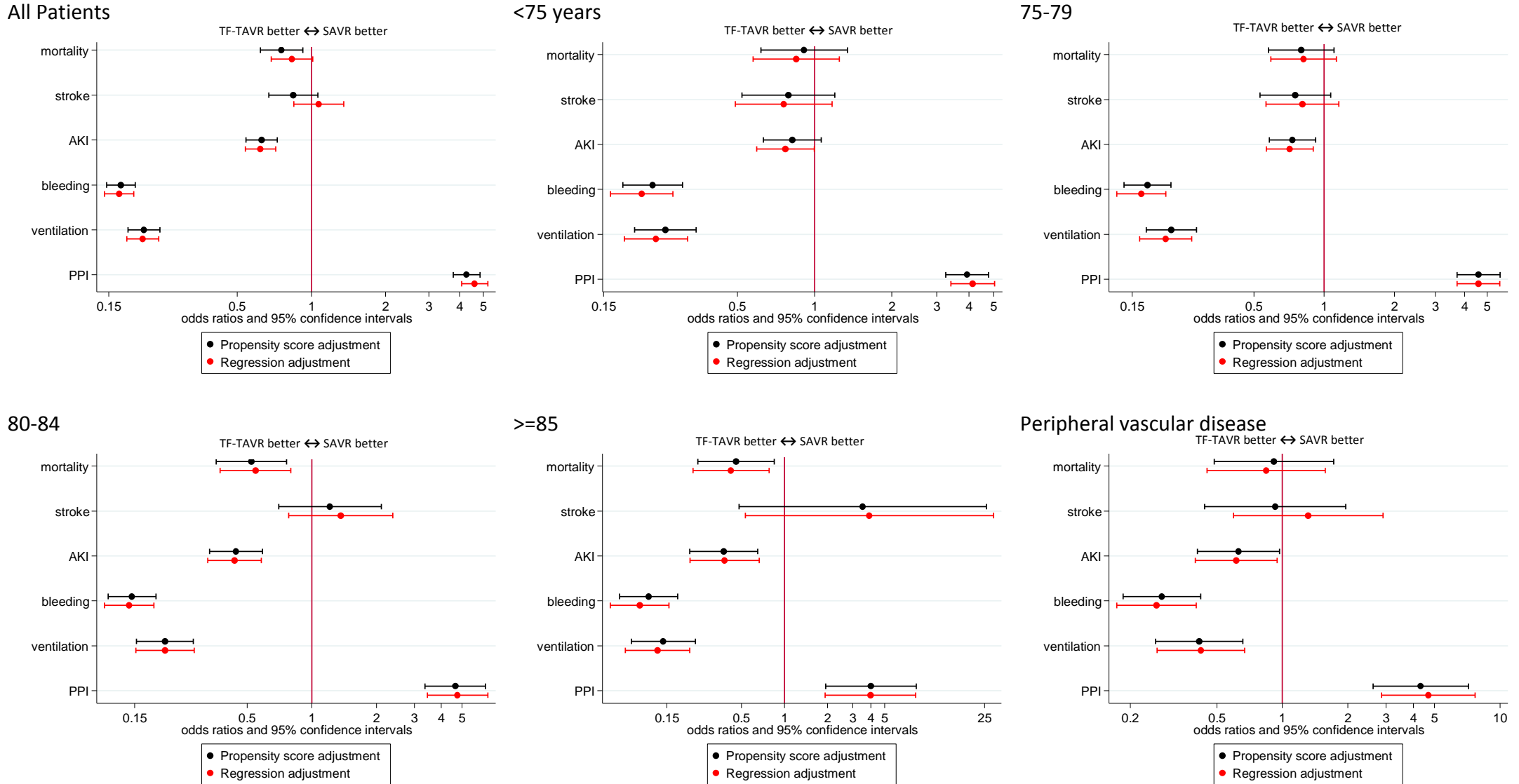
Analysis strategy 1: Covariate adjustment: Logistic regression models with a random intercept at the center level

Analysis strategy 2: Propensity score adjustment: First, a logistic regression model was performed on all patient and procedural characteristics to calculate the propensity score. The propensity score represents the likelihood that the patient was in the TF-TAVR arm. Then, logistic regression models

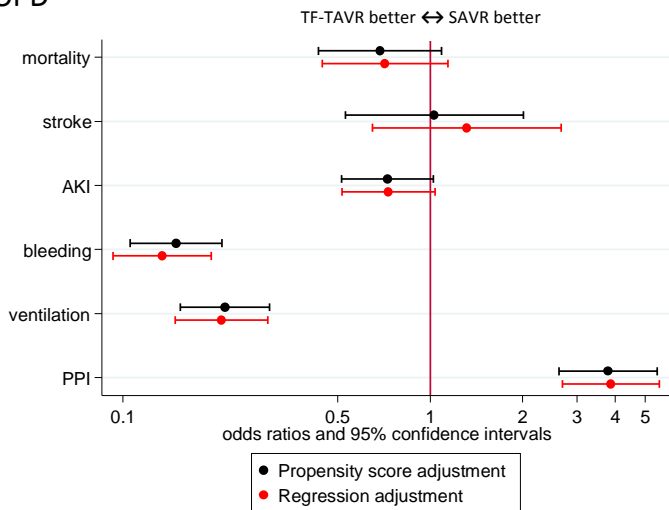
with a random intercept at the center level, the propensity score as continuous covariate and year 2015 as additional confounder were conducted.

SAVR: surgical aortic valve replacement; TF-TAVR: transfemoral transcatheter aortic valve replacement; SD: standard deviation; CAD: coronary artery disease; MI: myocardial infarction; CABG: coronary artery bypass graft; COPD: chronic obstructive pulmonary disease; GFR: glomerular filtration rate.

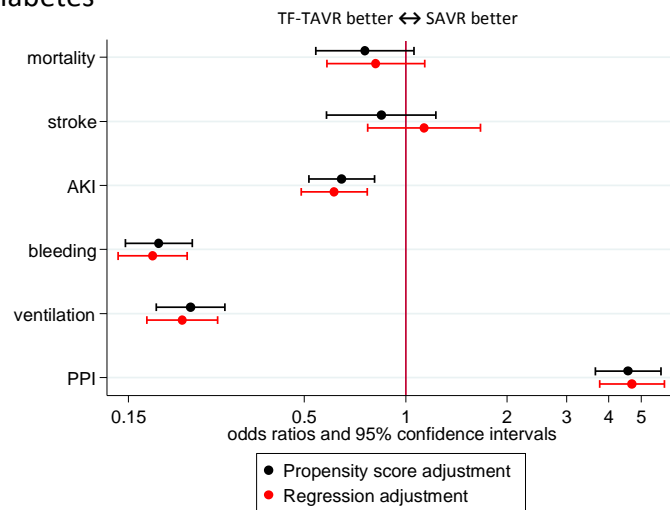
Figure S1. Results regarding different subgroups, outcomes and adjustment strategies



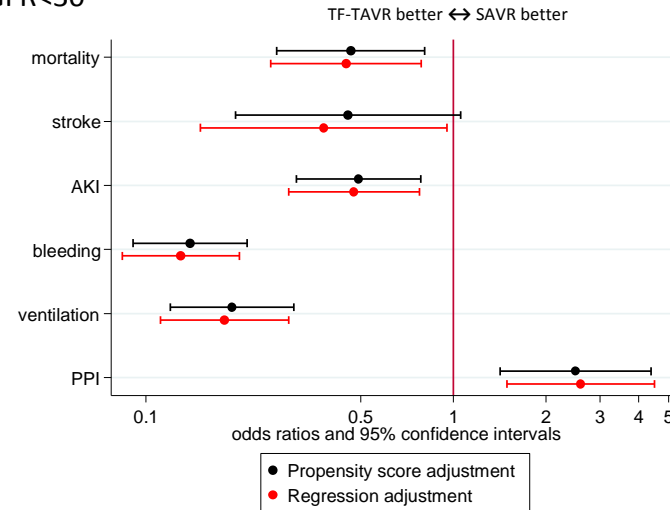
COPD



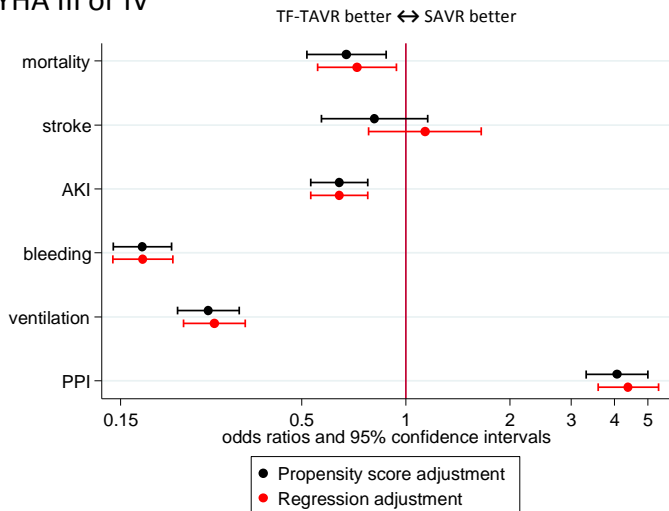
Diabetes



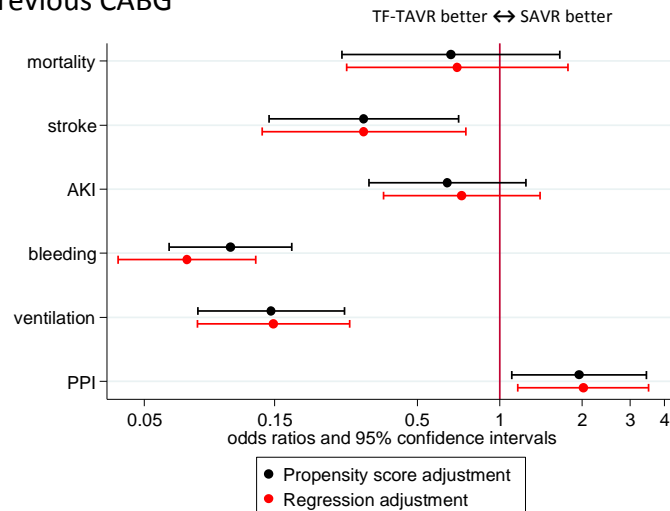
GFR<30



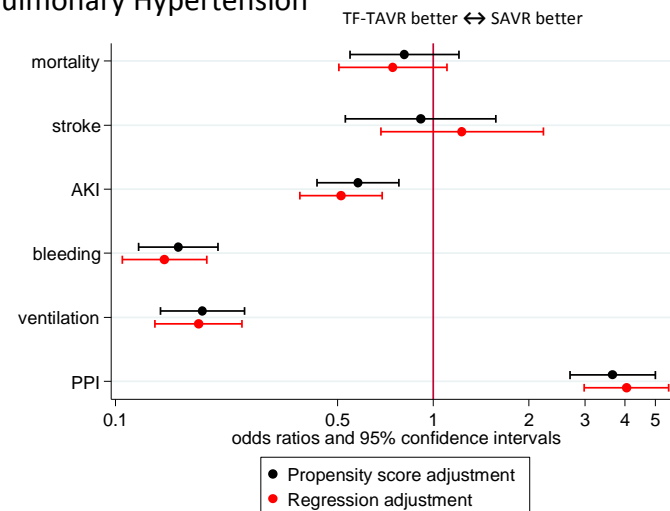
NYHA III or IV



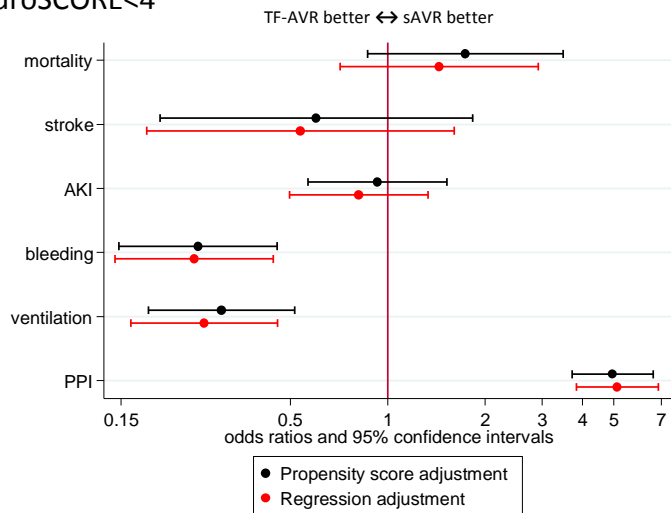
previous CABG



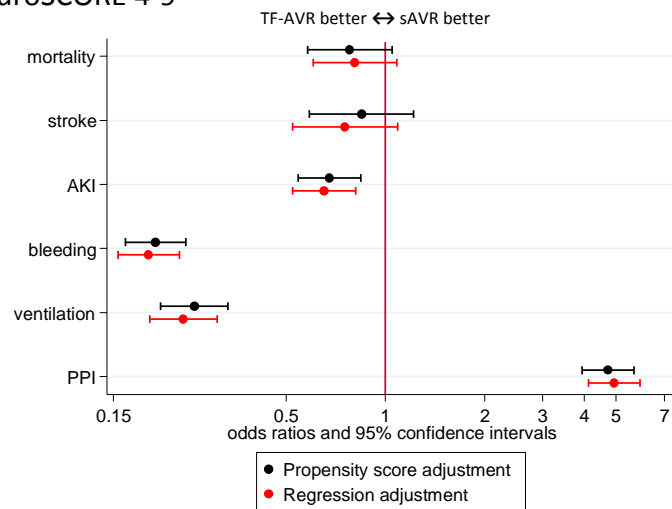
Pulmonary Hypertension



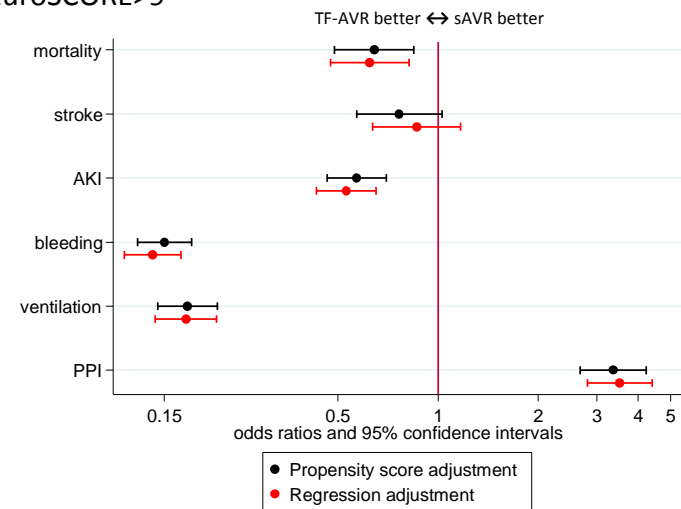
EuroSCORE<4



EuroSCORE 4-9



EuroSCORE>9



Female sex

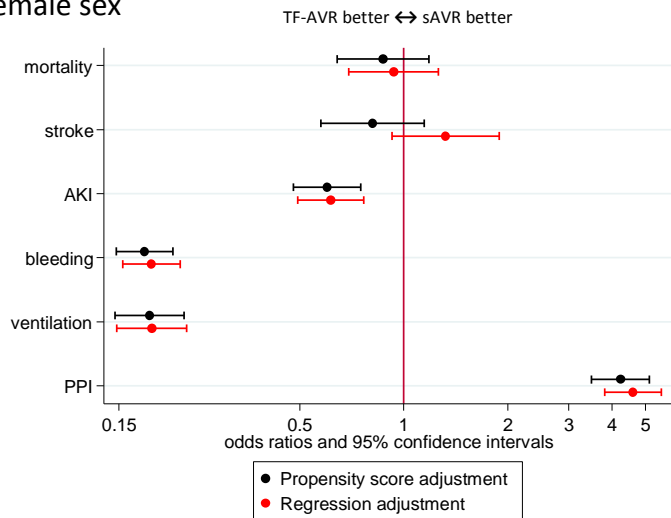


Figure S2.

