Incidence and outcomes of infective endocarditis after transcatheter aortic valve implantation versus surgical aortic valve replacement

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Incidence and Outcomes of Infective Endocarditis after Transcatheter Aortic Valve Implantation Versus Surgical Aortic Valve Replacement.

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Abstract

Objectives. Transcatheter aortic valve implantation (TAVI) is an alternative to surgical aortic valve replacement (AVR) in aortic stenosis (AS). Infective endocarditis (IE) in patients with prosthetic heart valves is associated with significant morbidity and mortality. Data on the incidence, risk factors, and outcomes of IE after TAVI are conflicting. We evaluated these issues in patients with percutaneous TAVI vs. isolated surgical AVR (SAVR) at a nationwide level.

Methods. Based on the administrative hospital-discharge database, the study collected information for all patients with aortic stenosis treated with AVR in France between 2010 and 2018.

Results. A total of 47,553 patients undergoing TAVI and 60,253 patients undergoing isolated SAVR were identified. During a mean follow-up of 2.0 years (median [25th to 75th percentile] 1.2 [0.1–3.4] years), the incidence rates of IE were 1.89 (95% confidence interval [CI] 1.78-2.00) and 1.40 (95%CI 1.34-1.46) events per 100 person-years in unmatched TAVI and SAVR patients, respectively. In 32,582 propensity-matched patients (16,291 with TAVI and 16,291 with SAVR), risk of IE was not different in patients treated with TAVI vs SAVR (incidence rates of IE 1.86 [95% CI 1.70-2.04] %/year vs 1.71 [95% CI 1.58-1.85] %/year respectively, relative risk [RR] 1.09, 95% CI 0.96-1.23). In these matched patients, total mortality was higher in TAVI patients with IE (43.0% 95%CI 37.3-49.3) than in SAVR patients with IE (32.8% 95%CI 28.6-37.3; RR 1.32, 95% CI 1.08-1.60).

Conclusion. In a nationwide cohort of patients with AS, treatment with TAVI was associated with a risk of IE similar to that following SAVR. Mortality was higher for patients with IE following TAVI compared to those with IE following SAVR.

Keywords: Aortic stenosis, Transcatheter aortic valve implantation, surgical aortic valve replacement, infective endocarditis.

Introduction

Continuous development has improved the results of transcatheter aortic valve implantation (TAVI) for severe aortic stenosis in high surgical risk patients.[1, 2] Recent data have also shown that TAVI is non-inferior to surgery in low- and intermediate-risk patients[3, 4]. The number of TAVI procedures has risen worldwide in recent years, and is expected to continue growing.[5]

Infective endocarditis (IE) in patients with prosthetic heart valves is associated with significant morbidity and mortality. Data on the incidence, risk factors, and outcomes of IE after TAVI are still limited and sometimes conflicting[6-8]. Considering some characteristics of patients eligible for TAVI (i.e., advanced age and high burden of comorbidities), these patients may be more likely to develop IE compared with those undergoing surgical aortic valve replacement (SAVR), although the TAVI procedure is less aggressive and hospital duration usually shorter than for SAVR. There is an inherent risk of nosocomial or healthcare acquisition of pathogens leading to IE directly linked to the transcatheter/surgical procedure, hospitalisation or other invasive procedures. The increasing number of patients with TAVI makes relevant to assess the clinical burden of this complication, to identify patients at high risk of IE and to evaluate the prognosis of patients with IE after TAVI.

Methods

Study design

This study was based on the national database covering hospital care from the entire French population. The data for all patients admitted with aortic stenosis in France from January 2010 to December 2018 were collected from the national administrative Programme de Médicalisation des Systèmes d'Information (PMSI) database. It includes more than 98% of the French population (67 million people) from birth (or immigration) to death (or

emigration), even if a person changes occupation or retires. Each hospitalisation is encoded in a standardised dataset, which includes information about the patient, hospital stay, pathologies, and procedures. Collected medical information includes the principal and secondary diagnoses coded according to the International Classification of Diseases, Tenth Revision (ICD-10). All medical procedures are recorded according to the national nomenclature, Classification Commune des Actes Medicaux (CCAM). The reliability of PMSI data has already been assessed[9] and validated for patients with IE[10], and this database has previously been used to study patients with cardiovascular conditions, including those with aortic stenosis treated with TAVI.[5, 11]

The study was conducted retrospectively and, as patients were not involved in its conduct, there was no impact on their care. Ethical approval was not required, as all data were anonymised. Procedures for data collection and management were approved by the Commission Nationale de l'Informatique et des Libertés (CNIL), the independent National Ethical Committee protecting human rights in France, which ensures that all information is kept confidential and anonymous (authorisation number 1897139).

Study population

From 1 January 2010 to 31 December 2018, 487,085 adults (age ≥18 years) were hospitalised with a diagnosis of aortic stenosis as the principal, related or significantly associated diagnosis. Patients with a history of IE were excluded of the analysis. For the analysis of SAVR procedures, we included all adults with a single procedure and we excluded patient with another concomitant open-heart procedure in addition to SAVR. For the analysis of TAVI procedures, we included all adults with a single percutaneous procedure. Patient information (demographics, comorbidities, procedures and events during hospitalisation or follow-up) was described using data collected in the hospital records. We also used the

EurosSCORE II, the Charlson Comorbidity Index and the Claims-based Frailty Indicator to assess patients' clinical status.[12-14] Exclusion criteria were age <18 years and TAVI via a non-percutaneous route.

Outcomes

Patients were followed until 31 December 2018 for the occurrence of outcomes. IE was identified when it was coded in the principal diagnosis or the associated diagnoses during follow-up (I330 using ICD10 codes). Mode of death (cardiovascular or non-cardiovascular) was identified based on the main diagnosis during hospitalisation resulting in death based on ICD-10 codes (for cardiovascular death: I00–I99 – Diseases of the heart and circulatory system).

Statistical analysis

Qualitative variables are described as counts and percentages and quantitative variable as means (standard deviations [SDs]) or median (interquartile range) where appropriate. Comparisons were made using chi-square tests for categorical variables and the Student *t* test or non-parametric Kruskal–Wallis test, as appropriate, for continuous variables. Owing to the non-randomised nature of the study, treatment selection bias and potential confounding were reduced by using propensity-score matching to account for significant differences in baseline characteristics. Propensity scores were calculated using logistic regression with valve type as the dependent variable. The propensity score included baseline characteristics listed in table 1 and year of implantation. For each patient with a TAVI, a propensity score-matched patient with SAVR was selected (1:1) using the one-to-one nearest neighbour method (with a calliper of 0.01 of the SD of the propensity score on the logit scale) and no replacement. We assessed the distributions of demographic data and comorbidities in the BE

and SE valve cohorts with standardized mean differences, which were calculated as the difference in the means or proportions of a variable divided by a pooled estimate of the SD of that variable. A standardized mean difference of 0.05 or less indicated a negligible difference between the means of the two cohorts.

For the outcomes analysis in the matched cohort, the incidence rates (%/year) for each outcome of interest during follow-up was estimated in TAVI and SAVR groups. The corresponding asymptotic two-sided 95% confidence interval (CI) of the relative risk (RR) was reported. A logistic regression model was used for the specific outcomes of death at 30 days and 1 year and odds ratio (OR) were reported. We performed a multivariable analysis in all patients using Cox proportional hazard risk model to compare the risk of outcomes between groups with hazard ratio (HR) and 95%CI. All comparisons with $p<0.05$ were considered statistically significant. Analyses were performed using Enterprise Guide 7·1, (SAS Institute Inc., SAS Campus Drive, Cary, North Carolina) and STATA version 12.0 (Stata Corp, College Station, TX).

Results

Baseline characteristics

Between 1 January 2010 and 31 December 2018, 107,806 patients were identified in the database, including 47,553 patients (44.1%) with TAVI and 60,253 patients (55.9%) with SAVR (figure 1). In the unmatched population, patients treated with TAVI were less frequently men, were older, and had higher Charlson comorbidity and frailty indexes. Patients treated with TAVI also had higher rates for most comorbidities. The propensity score had an area under ROC curve of 0.9215 (95%CI 0.9199-0.9231) for identifying the probability to be treated with TAVI. After propensity score matching, there were 16,291 patients in each group. Baseline characteristics in these populations were well matched (table

1).

Clinical outcomes

During a mean (SD) follow-up of 2.0 years (median [25th to 75th percentile] 1.2 [0.1–3.4] years), 8,981 patients (18.9%) with TAVI and 8,518 patients (14.1%) with SAVR died. In this unmatched population, 1,127 patients (2.4%) with TAVI and 2,125 patients (3.5%) with SAVR were admitted with IE. The incidence rates of IE were 1.89 (95% confidence interval [CI] 1.78-2.00) and 1.40 (95%CI 1.34-1.46) events per 100 person-years in unmatched TAVI and SAVR patients, respectively. Risk of IE was globally higher in patients treated with TAVI than SAVR (RR 1.35, 95%CI 1.26-1.45). In the matched populations, all-cause death was recorded in 2,862 patients (incidence rate 8.08%/year). All-cause death was higher in the TAVI group (table 2). Cardiovascular death was also higher in the TAVI group. In the matched population, 476 patients (4.4%) with TAVI and 594 patients (4.9%) with SAVR were admitted with IE. The incidence rates of IE were 1.86 (95% CI 1.70-2.04) and 1.71 (95% CI 1.58-1.85) events per 100 person-years in matched TAVI and SAVR patients, respectively. Risk of IE was not different in matched patients treated with TAVI or SAVR (RR 1.09, 95%CI 0.96-1.23) (table 2, figure 2). The median time from procedure to IE hospitalization was 398 days (interquartile 145 to 770 days) in the TAVI group and 469 days (interquartile 151 to 1,024 days) in the SAVR group. In the multivariable analysis in the unmatched population, adjusted risk of IE was also similar in patients treated with TAVI or SAVR (adjusted HR 0.97, 95%CI 0.86-1.09, p=0.58).

Table 3 shows factors associated with the development of IE in unmatched patients undergoing TAVI or SAVR. Male sex, Charlson comorbidity index, frailty index, atrial fibrillation, obesity, alcohol abuse and the presence of a cardiac implantable electronic device

were associated with a greater risk of IE. Male sex, Charlson comorbidity index, frailty index, atrial fibrillation and anaemia were associated with a greater risk of IE in TAVI patients. Male sex, Charlson comorbidity index, frailty index, obesity, alcohol abuse and the presence of a cardiac implantable electronic device were associated with a greater risk of IE in SAVR patients.

Characteristics of patients from the matched populations with a diagnosis of IE during follow-up are in table 4. Patients with TAVI and IE were slightly younger than those with SAVR and IE, other characteristics being similar. Of note, causative microorganisms were similar in the 2 groups of patients with IE treated with TAVI or SAVR. All-cause mortality was higher in patients with IE when they were initially treated with TAVI (43.0% 95%CI 37.3-49.3) compared to those treated with SAVR (32.8% 95%CI 28.6-37.3; RR 1.32, 95% CI 1.08-1.60) (table 2, figure 3). In the multivariable analysis in the whole population with IE (3,247 patients not limited to the TAVI patients matched to SAVR patients), adjusted risk of death was also higher in patients treated with TAVI compared to those treated with SAVR (adjusted HR 1.17, 95%CI 1.00-1.37, p=0.05).

Regarding surgical risk, we found a significant interaction for total mortality and cardiovascular death in the matched cohort (p for interaction <0.0001), with TAVI associated with a higher risk than SAVR, which was less marked in patients at higher risk (supplemental table 1). By contrast, there was no statistical interaction with surgical risk for incidence of IE during follow-up in matched patients treated with TAVI or SAVR, and for the subsequent risk of death once IE was diagnosed.

Discussion

This nationwide cohort study on the long-term risk of IE in patients undergoing percutaneous TAVI or isolated SAVR yielded the following major findings. First, TAVI was not associated

with a statistically significant different risk of IE compared with SAVR whilst TAVI is a much less invasive procedure than SAVR. Second, factors associated with a greater risk of IE in patients undergoing TAVI were not fully similar to those in patients undergoing SAVR. Third, in case of IE, mortality was higher for patients with TAVI compared to those with SAVR.

Some smaller or shorter studies have examined the short-term incidence of IE following TAVI[6, 16-24]. These data were in part conflicting, with a reported 1-year incidence of IE ranging from 0.5% to 3.4%. Possible explanations for these variations may be related to differences in risk profiles in patients across studies, different definitions of IE (i.e., possible IE or only definite IE, all cases of IE or only prosthetic valve IE), and a low number of patients in the many studies. The diagnosis may also be challenged by difficulties in echocardiography imaging in these patients. A meta-analysis of randomized trials in 3,761 did not find an increased risk of IE in TAVI compared with SAVR [25]. Recently, the pooled analysis of all patients in PARTNER 1 and PARTNER 2 trials and registries reported that IE remains rare but often fatal in modern SAVR experience and that there was no difference in incidence, predictors, or risk of IE between TAVI and SAVR.[26]

Identifying patients at high risk of IE following TAVI has significant implications for preventive efforts aiming to reduce the rate of IE. Factors associated with a greater risk of IE in patients undergoing TAVI had dissimilarities in comparison with those in patients undergoing SAVR in our analysis. Of note, the presences of diabetes, chronic kidney disease, or lung disease were not associated with IE whilst those factors are predictors of IE in many other settings. The higher prevalence of these comorbidities in patients with TAVI or SAVR, likely to be older than other patients with IE, may explain these findings. Potential strategies aiming at reducing the risk of IE in TAVI patients may specifically target frail male patients with atrial fibrillation or anaemia and might include closer surveillance, identification and

thorough management of infections, and reinforcement of preventive measures to reduce the risk of bacteraemia.

Streptococcus and staphylococcus were the most frequent causative microorganisms for IE in our patients. The rates of Staphylococcus aureus and coagulase-negative staphylococcus infection were comparable to those previously reported for patients with prosthetic valve IE or TAVI [27, 28], but lower than that reported by others[29]. In contrast to a prior large registry on TAVI[6], enterococci were not the most frequent causative microorganisms of IE after TAVI in our study. Our analysis also indicates that causative microorganisms were not different for patients with TAVI or SAVR. Considering the less aggressive nature of TAVI and usually shorter duration of hospital stay compared to SAVR, our results with similar incidences of IE in both groups of treatment raises questions on the appropriate prophylaxis of IE during follow-up after TAVI procedure, which might be more easily neglected. Health care providers should be aware that the risk of IE is not lower after TAVI than after SAVR.

TAVI was associated with a higher risk of death compared with SAVR in our matched analysis as in a smaller nationwide analysis[8]. IE following TAVI was associated with a poorer prognosis than IE in SAVR patients. The higher mortality in TAVI patients with IE compared with SAVR patients might also result from a conservative treatment in old patients with high prevalence of comorbidities, frequently at high-risk of cardiac surgery, even after the propensity-score matching. Since the prognosis was worse in TAVI than in SAVR patients as a whole, the prognosis after IE may also reflect the global outcomes in the 2 groups

Limitations

A main limitation of our study is inherent to the retrospective, observational nature of the

study and its potential biases. The study was based on administrative data, with limitations inherent to such methodology. Data were not systematically externally checked and this could have caused information bias. As coding of complications is linked to reimbursement and is regularly controlled, it is expected to be of good quality and it has been previously externally validated for IE[10]. Definite conclusions for comparisons between groups may not be fully appropriate even though multivariable matching was done, as it cannot fully eradicate the possible confounding variables between these groups. Our analysis was restricted to the variables present in the database, which meant that type of imaging modalities and characteristics such as mean gradient, valve area, calcification and vegetation were not available for analysis. We were not able to distinguish possible and definite IE as defined by the modified Duke criteria. Precise location of endocarditis (affected valve, native/prosthetic/or cardiac implantable electronic device-related IE) was not available with ICD codes. Thus, the comparison of IE incidence with the smaller studies studying specifically TAVI-IE or prosthetic valve IE after SAVR may not be fully appropriate. ICD codes do not allow distinguishing categories for causative microorganism. For example, *Streptococci* were categorized altogether (which include *S. viridans, S. gallolyticus* - associated with advanced age-, *S. agalactiae* and *dysgalactiae* harbouring higher aggressiveness). Another limitation is the lack of information on drug use, as drug therapies were not available in the database. This bias is possibly controlled by a relatively systematic use of similar antithrombotic strategies and drugs for heart failure in these patients based on current guidelines [1, 2].

Conclusions

Projections suggest that a rise in the number of TAVI procedures worldwide is inevitable.[17] Therefore, the outcomes and clinical events in patients treated with TAVI still need to be

thoroughly evaluated and our results on incidence, predictors and outcomes of IE after TAVI may provide some new and relevant insights for clinicians. There is probably room for improvement, including the prompt diagnosis of infective endocarditis in at-risk patients, and the early identification of patients with a highest risk of complications, as well as in the creation of multidisciplinary teams for the management of this disease.[30]

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Declaration of interests:

CSE reports honoraria from Abbott and Biotronik. DA has received fees for lectures or consulting from Amgen, Sanofi, Novartis, AstraZeneca, Bayer, Bristol-Myers Squibb, Boehringer-Ingelheim, MSD, Pfizer, and Servier. LF reports consultant or speaker activities for Bayer, BMS/Pfizer, Boehringer Ingelheim, Medtronic, and Novartis. TB reports consultant activities for Edwards Lifesciences. All other authors declare no competing interests.

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Figure legends

Figure 1. Flow chart of the study patients. SAVR = surgical aortic valve replacement; TAVI = transcatheter aortic valve implantation.

Figure 2. Kaplan-Meier event-free curves for incidence of infective endocarditis in matched patients undergoing TAVI and SAVR.

Figure 3. Kaplan-Meier event-free curves for total mortality in matched patients diagnosed with infective endocarditis following TAVI and SAVR. SAVR = surgical aortic valve replacement; TAVI = transcatheter aortic valve implantation.

Table 1. Baseline characteristics in the overall (unmatched) and matched populations treated with surgical aortic valve replacement or transcatheter aortic valve implantation

	Unmatched populations		SMD, TAVI vs SAVR (%)	p value	Matched populations		SMD, TAVI vs SAVR (%)	p value
	TAVI (n=47553)	SAVR (n=60253)			TAVI (n=16291)	SAVR (n=16291)		
Age, years	82.76±6.76	71.96±9.81	128.2	<0.0001	77.78±7.27	77.89±7.48	-1.3	0.19
Gender (male), n (%)	23072(48.5)	38248(63.5)	-30.5	<0.0001	9037(55.5)	9013 (55.3)	0.3	0.79
EuroSCORE II	3.68±0.96	3.30±1.07	37.5	<0.0001	3.57±1.04	3.55±1.01	2.2	0.06
Charlson comorbidity index	4.1±2.84	3.14±2.8	34.1	<0.0001	3.98±2.87	3.96±2.91	0.8	0.47
Frailty index	1.47±0.93	1.12±0.87	38.4	<0.0001	1.38±0.92	1.38±0.91	0.4	0.73
Hypertension	40245(84.6)	47537(78.9)	14.9	<0.0001	13632(83.7)	13720 (84.2)	-1.4	0.18
Diabetes mellitus	14677(30.9)	18554(30.8)	0.2	0.8	5501(33.8)	5465 (33.5)	0.5	0.67
Heart failure	27143(57.1)	20933(34.7)	46	<0.0001	7953(48.8)	8033 (49.3)	-1	0.38
History of pulmonary oedema	2607(5.5)	4970(8.2)	-11	<0.0001	1245(7.6)	1277 (7.8)	-0.8	0.51
Aortic regurgitation	5747(12.1)	7017(11.6)	1.4	0.03	2027(12.4)	2001 (12.3)	0.5	0.66
Mitral regurgitation	9081(19.1)	8046(13.4)	15.6	<0.0001	2906(17.8)	2883 (17.7)	0.4	0.74
Coronary artery disease	30924(65)	35630(59.1)	12.2	<0.0001	9808(60.2)	10065 (61.8)	-3.3	0.04
Previous myocardial infarction	6727(14.1)	5697(9.5)	14.6	<0.0001	2013(12.4)	2059 (12.6)	-0.9	0.44
Previous PCI	13516(28.4)	4750(7.9)	55.3	<0.0001	2483(15.2)	2500 (15.3)	-0.3	0.79
Vascular disease	17320(36.4)	16488(27.4)	19.5	<0.0001	5449(33.4)	5535 (34)	-1.1	0.31
Atrial fibrillation	21515(45.2)	29759(49.4)	-8.3	<0.0001	8014(49.2)	7933 (48.7)	1	0.37
Pacemaker or Defibrillator	9765(20.5)	3930(6.5)	41.9	<0.0001	2182(13.4)	2155 (13.2)	0.5	0.66
Stroke	2501(5.3)	1585(2.6)	13.5	<0.0001	665(4.1)	646 (4)	0.6	0.59
Smoker	4096(8.6)	8695(14.4)	-18.3	<0.0001	1963(12)	1882 (11.6)	1.6	0.16
Dyslipidaemia	23755(50)	33894(56.3)	-12.6	<0.0001	9001(55.3)	9067 (55.7)	-0.8	0.46
Obesity	12900(27.1)	19911(33)	-12.9	<0.0001	5317(32.6)	5400 (33.1)	-1.1	0.33
Alcohol related diagnoses	2372(5)	4104(6.8)	-7.7	<0.0001	1228(7.5)	1138 (7)	2.3	0.05
Abnormal renal function	8065(17)	3780(6.3)	33.8	<0.0001	1842(11.3)	1812 (11.1)	0.6	0.6
Lung disease	11418(24)	10321(17.1)	17.1	<0.0001	3958(24.3)	3822 (23.5)	2.1	0.08
Sleep apnoea syndrome	4019(8.5)	4508(7.5)	3.6	<0.0001	1572(9.6)	1544 (9.5)	0.6	0.6
Liver disease	2284(4.8)	2166(3.6)	6	<0.0001	941(5.8)	865 (5.3)	2.3	0.07
Thyroid diseases	6456(13.6)	4970(8.2)	17.2	<0.0001	1904(11.7)	1862 (11.4)	0.8	0.47
Inflammatory disease	4630(9.7)	3245(5.4)	16.5	<0.0001	1338(8.2)	1303 (8)	0.8	0.48

Anaemia	12882(27.1)	13041(21.6)	12.7	<0.0001	4025(24.7)	4021 (24.7)	0.1	0.96
Cancer within preceding 5 y	8627(18.1)	5771(9.6)	25	<0.0001	2556(15.7)	2465 (15.1)	1.6	0.16
Balloon Expandable TAVI	25708(54.1)	0(0)	-	-	8539(52.4)	0 (0)	-	-

Values are mean (SD) or n (%). CABG=coronary artery bypass graft; PCI=percutaneous coronary intervention; SAVR = surgical aortic valve replacement; SD=standard deviation; SMD, standardized mean difference; TAVI=transcatheter aortic valve implantation.

Table 2. Clinical outcomes in the matched cohort for patients treated with SAVR or TAVI

	TAVI (n=16291)	**SAVR (n=16291)**	**RR (95% CI) for TAVI vs SAVR**	**p**
All-cause death	3279 (12.60)	2862 (8.08)	1.56 (1.48-1.64)	<0.0001
Cardiovascular death	1339 (5.14)	1372 (3.87)	1.33 (1.23-1.43)	<0.0001
Infective endocarditis	476 (1.86)	594 (1.71)	1.09 (0.96-1.23)	0.17
All-cause death after a diagnosis of IE	205 (42.99)	225 (32.78)	1.32 (1.08-1.60)	0.005
All-cause death at day 30 after a diagnosis of IE	89 (18.70)	88 (14.81)	1.32 (0.96-1.83)*	0.09
All-cause death at 1 year after a diagnosis of IE	156 (32.77)	179 (30.13)	1.13 (0.87-1.47)*	0.36

Values are n (incidence rate, %/year). CI=confidence interval; IE = infective endocarditis; RR=incidence rate ratio; SAVR = surgical aortic valve replacement; TAVI=transcatheter aortic valve implantation. * values are odds ratios for All-cause death at day 30 and at 1 year.

Table 3. Hazard ratios for factors associated with infective endocarditis (A) Unmatched patients undergoing TAVI or SAVR. (B) Unmatched patients undergoing TAVI. (C) Unmatched patients undergoing SAVR.

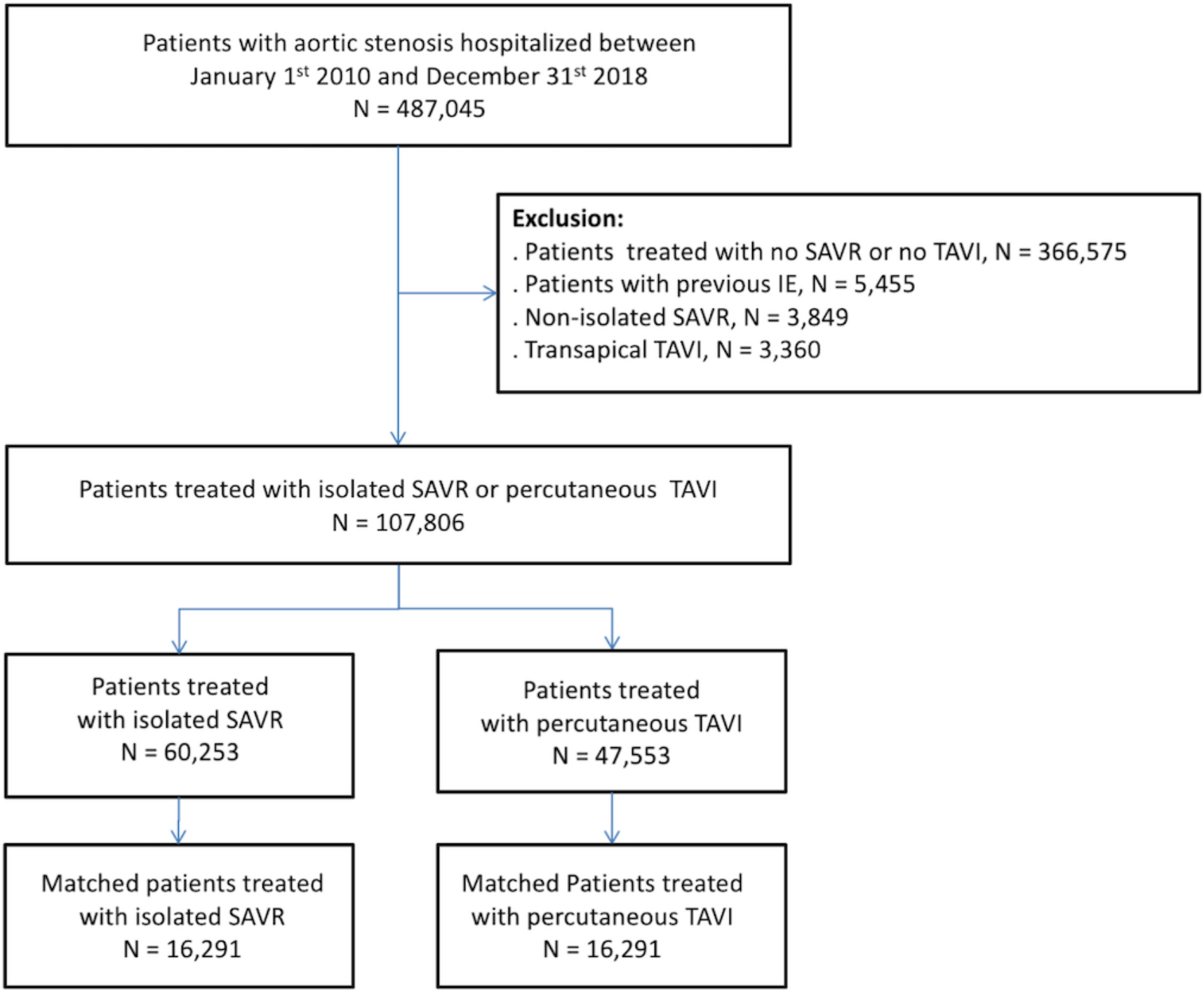
	Whole population with TAVI or SAVR		Patients with TAVI		Patients with SAVR	
	Hazard ratio, 95%CI	**p value**	**Hazard ratio, 95%CI**	**p value**	**Hazard ratio, 95%CI**	**p value**
Age, years	0.991, 0.987-0.995	<0.0001	0.978, 0.970-0.986	<0.0001	0.990, 0.985-0.995	<0.0001
Charlson comorbidity index	1.118, 1.101-1.135	<0.0001	1.073, 1.043-1.104	<0.0001	1.134, 1.114-1.155	<0.0001
Frailty index	1.320, 1.262-1.380	<0.0001	1.248, 1.157-1.346	<0.0001	1.348, 1.276-1.424	<0.0001
Gender (male), n (%)	1.590, 1.466-1.724	<0.0001	1.777, 1.558-2.028	<0.0001	1.511, 1.363-1.674	<0.0001
Hypertension	1.021, 0.911-1.144	0.73	1.053, 0.861-1.287	0.61	1.007, 0.877-1.157	0.92
Diabetes mellitus	0.812, 0.749-0.882	<0.0001	0.868, 0.755-0.997	0.05	0.783, 0.707-0.866	<0.0001
Heart failure	0.920, 0.850-0.995	0.04	0.907, 0.794-1.036	0.15	0.886, 0.802-0.978	0.02
History of pulmonary oedema	1.013, 0.878-1.168	0.86	0.972, 0.752-1.258	0.83	1.070, 0.899-1.273	0.45
Aortic regurgitation	1.000, 0.901-1.111	1.00	0.999, 0.843-1.184	0.99	1.000, 0.875-1.143	1.00
Mitral regurgitation	1.042, 0.943-1.151	0.42	1.072, 0.921-1.247	0.37	1.004, 0.879-1.146	0.96
Tricuspid regurgitation	1.124, 0.933-1.353	0.22	1.356, 1.032-1.782	0.03	0.974, 0.754-1.258	0.84
Coronary artery disease	1.028, 0.943-1.121	0.53	0.940, 0.813-1.088	0.41	1.072, 0.963-1.193	0.21
Previous myocardial infarction	1.052, 0.922-1.200	0.45	0.843, 0.685-1.037	0.11	1.230, 1.037-1.460	0.02
Previous PCI	0.954, 0.855-1.065	0.40	0.937, 0.808-1.088	0.40	0.914, 0.768-1.088	0.31
Previous CABG	0.817, 0.746-0.896	<0.0001	0.872, 0.713-1.066	0.18	0.818, 0.735-0.910	<0.0001
Vascular disease	0.760, 0.694-0.833	<0.0001	0.867, 0.749-1.004	0.06	0.696, 0.618-0.782	<0.0001
Atrial fibrillation	1.106, 1.030-1.188	0.005	1.226, 1.084-1.386	0.001	1.078, 0.987-1.179	0.10
Pacemaker or Defibrillator	1.138, 1.027-1.261	0.01	1.052, 0.915-1.210	0.47	1.163, 0.998-1.357	0.05
Stroke	0.773, 0.635-0.941	0.01	0.778, 0.587-1.032	0.08	0.783, 0.595-1.030	0.08
Smoker	0.954, 0.861-1.056	0.36	0.958, 0.790-1.161	0.66	0.940, 0.833-1.061	0.32
Dyslipidaemia	0.981, 0.910-1.058	0.62	0.976, 0.860-1.107	0.71	1.002, 0.911-1.101	0.98
Obesity	1.131, 1.047-1.222	0.002	1.125, 0.982-1.288	0.09	1.134, 1.031-1.246	0.009
Alcohol related diagnoses	1.219, 1.083-1.371	0.001	1.074, 0.854-1.351	0.54	1.248, 1.087-1.433	0.002
Abnormal renal function	0.937, 0.837-1.049	0.26	0.912, 0.779-1.067	0.25	0.936, 0.793-1.105	0.44

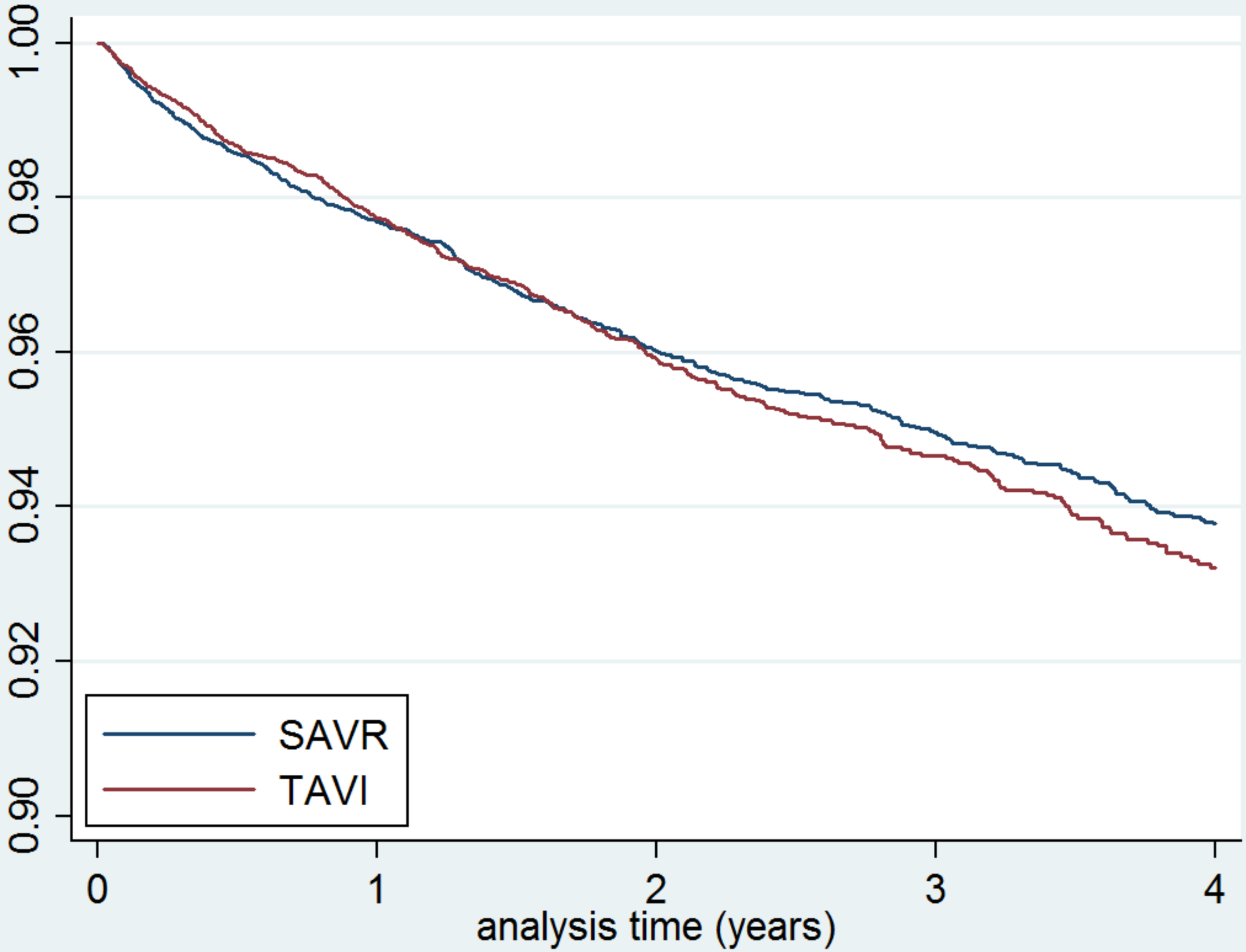
Lung disease	0.910, 0.836-0.991	0.03	0.860, 0.749-0.987	0.03	0.926, 0.830-1.032	0.17
Sleep apnoea syndrome	1.081, 0.958-1.221	0.21	1.095, 0.897-1.337	0.37	1.045, 0.896-1.219	0.58
Liver disease	0.980, 0.835-1.152	0.81	1.023, 0.797-1.314	0.86	0.921, 0.741-1.145	0.46
Thyroid diseases	1.025, 0.908-1.157	0.69	1.155, 0.972-1.372	0.10	0.890, 0.749-1.058	0.19
Inflammatory disease	0.951, 0.832-1.086	0.46	0.970, 0.802-1.174	0.76	0.917, 0.760-1.107	0.37
Anaemia	1.046, 0.964-1.134	0.28	1.262, 1.107-1.438	<0.0001	0.937, 0.844-1.041	0.23
Cancer within preceding 5 y	0.945, 0.851-1.048	0.28	1.015, 0.870-1.185	0.85	0.858, 0.741-0.993	0.04

CABG=coronary artery bypass graft; PCI=percutaneous coronary intervention; SAVR = surgical aortic valve replacement; TAVI=transcatheter aortic valve implantation.

Table 4. Baseline characteristics in the matched patients treated with surgical aortic valve replacement or transcatheter aortic valve implantation with a diagnosis of infective endocarditis during follow-up.

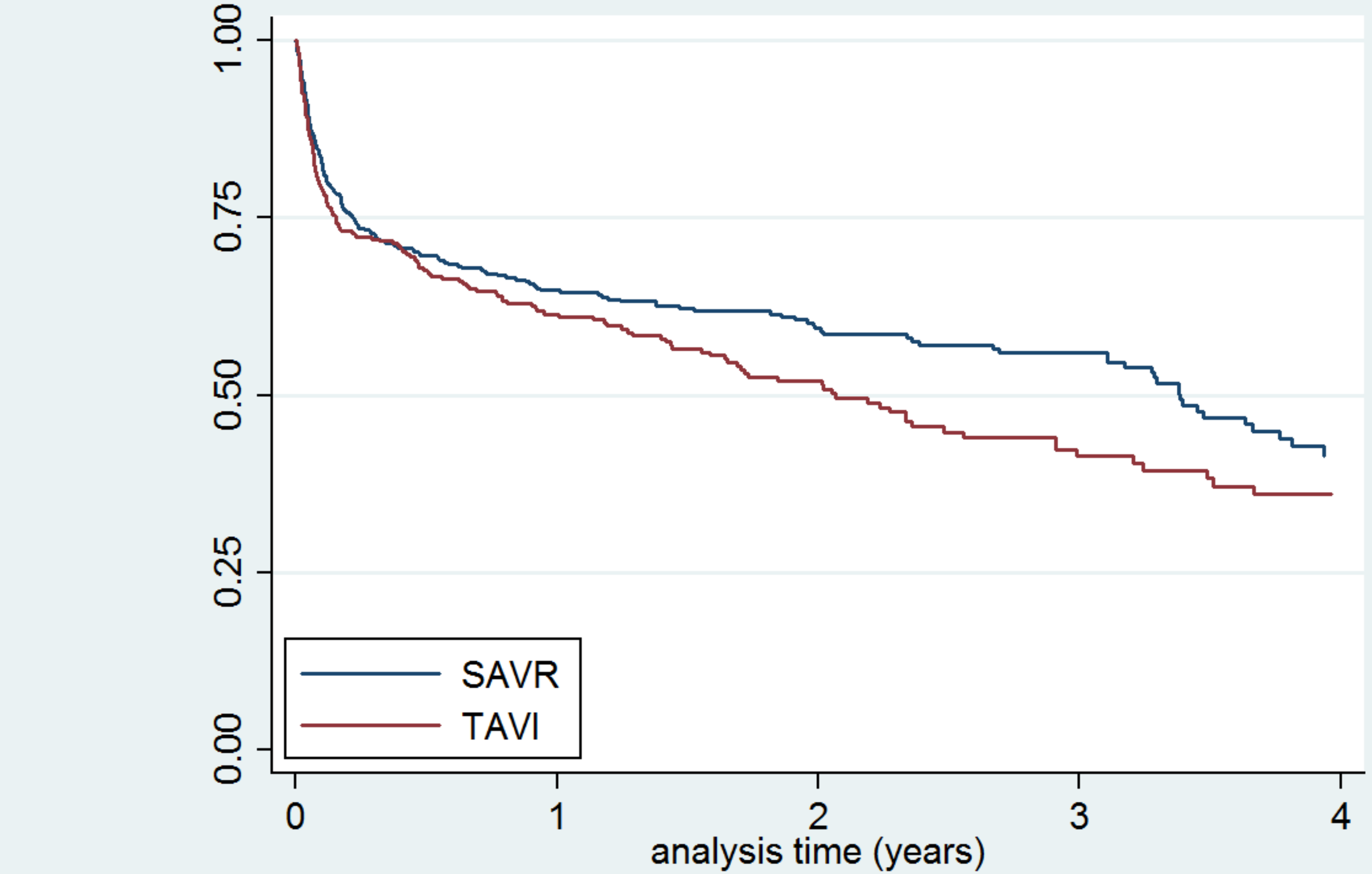
	TAVI (n=476)	**SAVR (n=594)**	**p**
Age, years	76.01±7.95	77.71±7.46	0.0003
Gender (male), n (%)	312(65.5)	394(66.3)	0.79
EuroSCORE II	3.61±1.04	3.54±1.02	0.3
Charlson comorbidity index	5.94±3.09	5.7±2.98	0.2
Frailty index	1.92±0.87	1.94±0.89	0.69
Gender (male), n (%)	312(65.5)	394(66.3)	0.79
Hypertension	432(90.8)	531(89.4)	0.46
Diabetes mellitus	193(40.5)	234(39.4)	0.7
Heart failure	273(57.4)	319(53.7)	0.23
History of pulmonary oedema	33(6.9)	35(5.9)	0.49
Aortic regurgitation	64(13.4)	81(13.6)	0.93
Mitral regurgitation	97(20.4)	100(16.8)	0.14
Tricuspid regurgitation	22(4.6)	30(5.1)	0.75
Coronary artery disease	302(63.4)	396(66.7)	0.27
Previous myocardial infarction	56(11.8)	71(12)	0.92
Previous PCI	66(13.9)	79(13.3)	0.79
Previous CABG	83(17.4)	102(17.2)	0.91
Vascular disease	159(33.4)	188(31.6)	0.54
Atrial fibrillation	255(53.6)	310(52.2)	0.65
Pacemaker or Defibrillator	76(16)	108(18.2)	0.34
Stroke	15(3.2)	19(3.2)	0.97
Smoker	79(16.6)	83(14)	0.23
Dyslipidaemia	279(58.6)	358(60.3)	0.58
Obesity	191(40.1)	234(39.4)	0.81
Alcohol related diagnoses	67(14.1)	75(12.6)	0.49
Abnormal renal function	75(15.8)	71(12)	0.07
Lung disease	145(30.5)	172(29)	0.59
Sleep apnea syndrome	62(13)	59(9.9)	0.11
Liver disease	45(9.5)	39(6.6)	0.08
Thyroid diseases	56(11.8)	57(9.6)	0.25
Inflammatory disease	34(7.1)	44(7.4)	0.87
Anaemia	151(31.7)	154(25.9)	0.04
Cancer within preceding 5 y	95(20)	108(18.2)	0.46
Causative microorganism:			
Staphylococcus aureus	75(15.8)	103(17.3)	0.49
Coagulase-negative Staphylococcus	63(13.2)	92(15.5)	0.3
Streptococcus	138(29)	144(24.2)	0.08
Enterococcus	108(22.7)	126(21.2)	0.56
Others	34(7.1)	51(8.6)	0.39


Patients with aortic stenosis hospitalized between
January 1st 2010 and December 31st 2018
N = 487,045
Exclusion:
. Patients treated with no SAVR or no TAVI, N = 366,575
. Patients with previous IE, N = 5,455
. Non-isolated SAVR, N = 3,849
. Transapical TAVI, N = 3,360
Patients treated with isolated SAVR or percutaneous TAVI
N = 107,806
Patients treated
with isolated SAVR
N = 60,253
Patients treated
with percutaneous TAVI
N = 47,553
Matched patients treated
with isolated SAVR
N = 16,291
Matched Patients treated
with percutaneous TAVI
N = 16,291



Number at risk

SAVR 16247	9144	7007	5177	3573
TAVI 16132	7807	5217	3287	1929



Number at risk

SAVR	594	212	143	87	30
TAVI	476	157	87	45	27