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Prosthetic valve endocarditis after transcatheter or surgical aortic valve replacement with a bioprosthesis: results from the FinnValve Registry

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KEYWORDS

- aortic stenosis
- miscellaneous
- TAVI

Abstract

Aims: The aim of this study was to compare the risk of prosthetic valve endocarditis (PVE) in patients with transcatheter aortic valve replacement (TAVR) or surgical aortic valve replacement (SAVR).

Methods and results: The FinnValve registry included data from 6,463 consecutive patients who underwent TAVR (n=2,130) or SAVR (n=4,333) with a bioprosthesis from 2008 to 2017. PVE was defined according to the modified Duke criteria. In this study, the incidence of PVE was 3.4/1,000 person-years after TAVR, and 2.9/1,000 person-years after SAVR. In competing risk analysis there was no significant difference in the risk of PVE between patients with TAVR and SAVR over an eight-year observational period. Male gender (HR 1.73, 95% CI: 1.04-2.89) and deep sternal wound infection or vascular access-site infection (HR 5.45, 95% CI: 2.24-13.2) were positively associated with PVE, but not type of procedure (HR 1.09, 95% CI: 0.59-2.01) in multivariate analysis. The mortality rate was 37.7% at one month and increased to 52.5% at one year. Surgical treatment was independently associated with decreased in-hospital mortality (HR 0.34, 95% CI: 0.21-0.61).

Conclusions: PVE is rare, and its risk is similar after TAVR and SAVR. ClinicalTrials.gov Identifier: NCT03385915. https://clinicaltrials.gov/ct2/show/NCT03385915

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Abbreviations

AS aortic stenosis
AVR aortic valve replacement
PVE prosthetic valve endocarditis
SAVR surgical aortic valve replacement
TAVR transcatheter aortic valve replacement

Introduction

Prosthetic valve endocarditis (PVE) has been described as being a causative factor of bioprosthetic valve dysfunction[1,2]. PVE is rare but is associated with a high mortality rate[3,4]. The clinical features and outcomes associated with PVE have been well documented in patients undergoing surgical aortic valve replacement (SAVR)[5,6], while data on PVE after transcatheter aortic valve replacement (TAVR) are currently very limited.

TAVR has become the dominant treatment strategy for severe aortic stenosis (AS) in patients at high and intermediate risk[7-10]. During the past few years, clinical practice has shifted towards also treating lower-risk patients with TAVR[11,12]. Accordingly, extended knowledge of the durability of TAVR is essential when considering expanding the indication for TAVR to patients with lower risk and those with long life expectancy[13]. Therefore, the long-term data on bioprosthetic valve dysfunction due to PVE after TAVR are emerging. We sought to investigate 1) the long-term risk of PVE after TAVR in comparison to SAVR, and 2) the clinical outcomes after PVE in the FinnValve registry.

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Methods

STUDY DESIGN

The FinnValve registry is a nationwide registry, which includes retrospectively collected data from consecutive and unselected patients who underwent TAVR or SAVR with a bioprosthesis for AS at all five Finnish university hospitals (Helsinki, Kuopio, Oulu, Tampere and Turku) from January 2008 to October 2017. This study was approved by the institutional review boards of each participating centre. The inclusion and exclusion criteria are shown in **Supplementary Table 1**. The operative risk of the patients was evaluated according to the Society of Thoracic Surgeons (STS-PROM)[14] and the EuroSCORE II[15] risk scoring methods.

Data were retrospectively collected into a dedicated electronic case report form. Data underwent robust checking of their completeness and quality. Data on date and cause of death were obtained from the national registry Statistics Finland, which is based on death certificates reviewed by local and central authorities. Based on this information, follow-up was considered complete for all patients, except for two patients who were not residing in Finland and for whom follow-up was truncated at hospital discharge.

DEFINITIONS

The definition of PVE was based on the modified Duke criteria[16]. Cases with definite and possible infective endocarditis (IE) involving the aortic valve prosthesis were considered in this analysis. Any cases considered possible IE were evaluated and finally either included or not in the study on the basis of a consensus of three investigators (N. Moriyama, T. Laakso and M. Laine). Evidence of typical findings of PVE was confirmed by imaging, surgical inspection, or pathological evaluation.

Baseline variables were defined according to the EuroSCORE II criteria[15]. Frailty was defined according to the geriatric status scale (GSS); herein GSS grades 2-3 were defined as severe[17].

OUTCOME MEASURES

The primary outcome of the study was to define the risk of PVE after TAVR and SAVR. The secondary outcomes were the early adverse events and survival after PVE listed in **Table 1** and **Table 2**.

Major bleeding was defined as European multicentre study on coronary artery bypass grafting (E-CABG) bleeding grade 2-3[18] together with the Valve Academic Research Consortium (VARC)-2 definition of life-threatening and major bleeding. Acute kidney injury (AKI) was defined according to the KDIGO classification criteria[19], because it considers a time frame for creatinine changes of seven days, which is usually the average length of hospital stay in patients undergoing SAVR. Other outcomes were defined according to the VARC-2 criteria[20]. The early outcomes were defined as periprocedural and post-procedural outcomes during the hospital stay for the indexed aortic valve replacement (AVR).

STATISTICAL ANALYSIS

Categorical variables are presented as counts and/or percentages and were compared using the chi-square test. Continuous variables are presented as the mean±standard deviation (SD) or interquartile range (IQR) and were compared using the Student's t-test or Mann-Whitney U test based on their distributions. Differences in baseline covariates between treatment groups were adjusted using one-to-one propensity score matching analysis with a calliper width of 0.2 of the standard deviation of logit **(Supplementary Appendix 1)**. The risk of PVE was then estimated using competing risk analysis. In competing risk terms, any PVE corresponds to the event of interest. The competing risk was death before PVE. We used cumulative incidence function (CIF) to display the proportion of patients with the event of interest or the competing event as time progressed[21]. To evaluate the effect of baseline predictors including early outcomes after TAVR or SAVR on the CIF, the Fine and Gray regression model for the sub-distribution hazard was applied[22]. The following covariates with $p<0.20$ in univariate analysis were included in the model: age, gender, estimated glomerular filtration rate (eGFR), chronic obstructive pulmonary disease (COPD), active malignancy, critical preoperative state, moderate-to-severe paravalvular regurgitation, reoperation for mediastinal or peripheral bleeding, and deep sternal wound infection (DSWI) or vascular access-site infection. A multivariate analysis was performed to determine the independent predictors of the incidence of PVE. The covariates with $p<0.20$ in univariate analysis (gender, eGFR, COPD, Frailty GSS 2 to 3, SAVR, DSWI or vascular access-site infection and reoperation for mediastinal or

Table 1. Baseline characteristics and early outcomes in patients with or without aortic prosthetic valve endocarditis.

Variables		Overall (n=6,463)	PVE (n=68)	No PVE (n=6,395)	*p*-value
Baseline characteristics					
Age, yrs		77.1±7.2	76.3±8.5	77.1±7.1	0.52
Female		3,198 (49.5)	25 (36.8)	3,173 (49.6)	0.027
Body mass index, kg/m^2		27.5±4.8	27.3±4.8	27.5±4.8	0.88
Haemoglobin, g/l		130±15	130±17	130±15	0.99
eGFR, ml/min/1.73 m^2		72±23	77±23	72±23	0.14
Dialysis		38 (0.6)	1 (1.4)	37 (0.6)	0.28
Diabetes		1,759 (27.2)	20 (29.4)	1,739 (27.2)	0.62
COPD		1,098 (17.0)	18 (26.5)	1,080 (16.9)	0.032
Atrial fibrillation		1,887 (29.2)	22 (32.4)	1,865 (29.2)	0.39
Extracardiac arteriopathy		951 (14.7)	11 (16.2)	940 (14.7)	0.70
Coronary artery disease		2,573 (39.8)	30 (44.1)	2,543 (39.8)	0.46
Active malignancy		144 (2.2)	0	144 (2.3)	<0.001
Prior pacemaker implantation		382 (5.9)	6 (8.6)	376 (5.9)	0.49
Prior cardiac surgery		528 (8.2)	5 (7.4)	523 (8.2)	0.88
Prior PCI		872 (13.5)	7 (10.3)	865 (13.5)	0.59
Frailty GSS ≥2		425 (6.6)	1 (1.5)	424 (6.6)	0.16
Critical preoperative state		161 (2.5)	0	161 (2.5)	<0.001
NYHA Class IV		697 (10.7)	6 (8.8)	691 (10.8)	0.59
LVEF ≤50%		1,505 (23.3)	19 (27.9)	1,486 (23.3)	0.38
Bicuspid aortic valve		1,034 (16.0)	10 (14.7)	1,024 (16.0)	0.78
Urgent or emergent procedure		746 (11.5)	6 (8.8)	740 (11.6)	0.45
TAVR		2,130 (33.0)	15 (22.1)	2,115 (33.1)	0.45
EuroSCORE II, %		5.2±6.4	4.3±4.0	5.2±6.4	0.19
STS score, %		3.6±3.1	3.1±2.3	3.6±3.1	0.22
Early outcomes					
Moderate to severe PVL		108 (1.7)	2 (2.9)	106 (1.6)	0.38
New pacemaker implantation		355 (5.5)	1 (1.5)	354 (5.5)	0.20
Stroke		218 (3.4)	3 (4.4)	215 (3.4)	0.66
Major vascular complication		260 (4.0)	3 (4.4)	257 (4.0)	0.67
RBC transfusion		3,413 (53.6)	40 (59.7)	3,373 (53.5)	0.94
RBC transfusion, units		2.2±3.5	2.6±3.0	2.2±3.5	0.87
Reoperation for mediastinal or peripheral bleeding		432 (6.7)	2 (2.9)	430 (6.7)	0.20
E-CABG bleeding grades 2-3		1,149 (17.8)	16 (23.9)	1,133 (18.0)	0.46
VARC-2 bleeding	Major	2,131 (33.1)	26 (38.2)	2,105 (33.0)	0.24
	Life-threatening	2,764 (42.9)	33 (48.5)	2,731 (42.8)	0.37
Acute kidney injury	Stage 1	690 (10.7)	4 (6.0)	686 (10.9)	0.15
	Stage 2	162 (2.5)	1 (1.5)	161 (2.6)	0.49
	Stage 3	148 (2.3)	3 (4.5)	145 (2.3)	0.38
Infectious complications		886 (13.7)	11 (16.2)	875 (13.7)	0.59
DSWI or vascular access-site infection		103 (1.6)	6 (8.8)	97 (1.5)	<0.001
DSWI		63 (1.0)	3 (4.4)	60 (0.9)	0.014
Vascular access-site infection		41 (0.6)	3 (4.4)	38 (0.6)	0.001
Length of hospital stay, days		7.4±6.2	8.7±6.9	7.4±6.1	0.17

Values are expressed as n (%) or mean±standard deviation (SD). P-values were generated by competing risk analysis. CABG: coronary artery bypass grafting; COPD: chronic obstructive pulmonary disease; DSWI: deep sternal wound infection; E-CABG: European multicentre study on coronary artery bypass grafting; eGFR: estimated glomerular filtration rate; GSS: geriatric status scale; LVEF: left ventricular ejection fraction; NYHA: New York Heart Association; PCI: percutaneous coronary intervention; PVE: prosthetic valve endocarditis; PVL: paravalvular leakage; RBC: red blood cell; STS: Society of Thoracic Surgeons; TAVR: transcatheter aortic valve replacement; VARC-2: Valve Academic Research Consortium-2

Table 2. Prosthetic valve endocarditis features and in-hospital outcomes in patients with TAVR or SAVR.

		All PVE (n=68)	TAVR-PVE (n=15)	SAVR-PVE (n=53)	*p*-value
Age at admission for PVE		78.4±8.1	85.1±9.0	76.5±6.7	<0.001
First symptoms	Fever	49 (72.1)	13 (86.7)	36 (67.9)	0.15
	Sepsis	18 (26.5)	4 (26.7)	14 (26.4)	0.98
	Heart failure	7 (10.3)	2 (13.3)	5 (9.4)	0.66
	Bradycardia	4 (5.9)	1 (6.7)	3 (5.7)	0.88
	Neurological	2 (2.9)	0 (0)	2 (3.8)	0.45
	Weight loss	2 (2.9)	0 (0)	2 (3.8)	0.45
NYHA ≥III at admission		27 (39.7)	5 (33.3)	22 (41.5)	0.57
Possible causative event	Infection	23 (33.8)	6 (40.0)	17 (32.1)	0.57
	Dental	3 (4.4)	1 (6.7)	2 (3.8)	0.63
	Urologic tract	11 (16.2)	1 (6.7)	10 (18.9)	0.25
	Intestinal tract	4 (5.9)	2 (13.3)	2 (3.8)	0.16
	Skin	3 (4.4)	0 (0)	3 (5.7)	0.34
	Surgery*	12 (17.7)	2 (13.3)	10 (18.9)	0.62
	Unknown	28 (41.2)	5 (33.3)	23 (43.3)	0.49
Onset to diagnosis, days	Mean	56.5±85.6	40.5±79.2	61.3±87.4	0.39
	Median	22 (5-49)	7 (2-20)	27 (7-52)	–
Modified Duke criteria	Definite	57 (83.8)	12 (80.0)	45 (84.9)	0.65
	Possible	11 (16.2)	3 (20.0)	8 (15.1)	0.65
Causative microorganism(s)	Staphylococci	26 (38.2)	4 (26.7)	22 (41.5)	0.30
	Coagulase-positive	11 (16.1)	3 (20.0)	8 (15.1)	0.65
	Coagulase-negative	15 (22.1)	1 (6.8)	14 (26.4)	0.10
	Enterococci	13 (19.1)	4 (26.7)	9 (17.0)	0.40
	Streptococci	19 (27.9)	7 (46.7)	12 (22.6)	0.049
	Fungal	1 (1.4)	0 (0)	1 (1.9)	0.59
	BCNIE	4 (5.9)	0 (0)	4 (7.6)	0.27
	Others	5 (7.4)	0 (0)	5 (9.4)	0.22
Echocardiographic finding(s)		55 (80.9)	8 (53.3)	47 (88.7)	0.002
Vegetation		40 (58.9)	6 (40.0)	34 (64.2)	0.093
Abscess		17 (25.0)	0 (0)	17 (32.1)	0.011
Leaflet dehiscence		6 (8.8)	0 (0)	6 (11.3)	0.17
Fistula		4 (5.8)	0 (0)	4 (7.6)	0.27
Pseudoaneurysm		2 (2.9)	0 (0)	2 (3.8)	0.46
New aortic regurgitation ≥2 grade		19 (27.9)	5 (33.3)	4 (26.2)	0.60
New mitral regurgitation ≥2 grade		15 (22.1)	3 (20.0)	12 (22.6)	0.83
Embolisation(s)		18 (26.5)	1 (6.7)	17 (32.1)	0.051
Brain		13 (19.1)	1 (6.7)	12 (22.6)	0.16
Spleen		4 (6.3)	0 (0)	4 (7.5)	0.27
Others		5 (8.1)	0 (0)	5 (10.4)	0.21
Surgical treatment		26 (38.2)	1 (6.7)	25 (47.2)	0.004
In-hospital death		19 (27.9)	3 (20.0)	17 (32.1)	0.44

Values are expressed as n (%), mean±standard deviation (SD), or median (IQR). *Any surgical procedures including permanent pacemaker implantation. BCNIE: blood culture negative infective endocarditis; NYHA: New York Heart Association; PVE: prosthetic valve endocarditis; SAVR: surgical aortic valve replacement; TAVR: transcatheter aortic valve replacement

peripheral bleeding **[Table 1]** and age) were included in the multivariate analysis. Factors at onset of PVE were also analysed to evaluate the risk factors of mortality in patients with PVE using multivariable Cox proportional hazards analysis. Age at the time of PVE was tested as an effect modifier for the relevant covariates. Variables with p<0.2 in univariate analysis were selected for the multivariable analysis. The cumulative mortality and PVE were presented as Kaplan-Meier curves. All hypothesis testing was two-sided with a significance level of 0.05. Statistical analysis was performed using SAS statistical package version 9.2 (SAS Institute Inc., Cary, NC, USA), SPSS, Version 25.0 statistical software (IBM Corp., Armonk, NY, USA) and Stata v. 15.1 statistical software (StataCorp LLC, College Station, TX, USA).

Results

The FinnValve registry includes 6,463 patients who underwent primary TAVR or SAVR with a bioprosthesis for AS: 2,130 (33.0%) patients underwent TAVR and 4,333 (67.0%) underwent SAVR **(Supplementary Figure 1)**. The mean follow-up was 3.5±2.6 years (median 3.0, IQR 1.3-5.2 years, range 0-10.0 years) in the overall cohorts, 3.1±1.7 years in the TAVR cohort, and 4.2±2.6 years in the SAVR cohort.

PROPENSITY SCORE MATCHING MODEL

TAVR and SAVR groups differed in most baseline covariates as shown by standardised differences **(Supplementary Table 2)**. Propensity score matching provided 1,252 pairs with similar characteristics (STS score: TAVR 3.9±2.6% vs SAVR 4.1±3.7%, p=0.22, EuroSCORE II: TAVR 5.4±5.6% vs SAVR 5.6±6.6%, p=0.14) as well as standardised differences <0.1 for all covariates. Among the matched pairs, the competing risk analysis showed that the risk of PVE was similar between the study groups (SAVR vs TAVR, HR 1.67, 95% CI: 0.61-4.59) **(Supplementary Figure 2)**.

OVERALL SERIES

A total of 68 cases of PVE were identified including 15 PVEs in the TAVR and 53 PVEs in the SAVR cohort. The mean time between the indexed AVR and the diagnosis of PVE was 2.1±2.4 years. The overall incidence of PVE was 3.0/1,000 person-years (3.4/1,000 person-years after TAVR, and 2.9/1,000 person-years after SAVR). The main baseline characteristics and early outcomes of patients who experienced PVE are summarised in **Table 1**. No significant difference in the risk of PVE between TAVR and SAVR was observed over an observational period **(Figure 1)**.

Multivariate analysis showed that male gender (HR 1.73, 95% CI: 1.04-2.89) and DSWI or vascular access-site infection (HR 5.45, 95% CI: 2.24-13.2) were independently associated with PVE **(Figure 2)**.

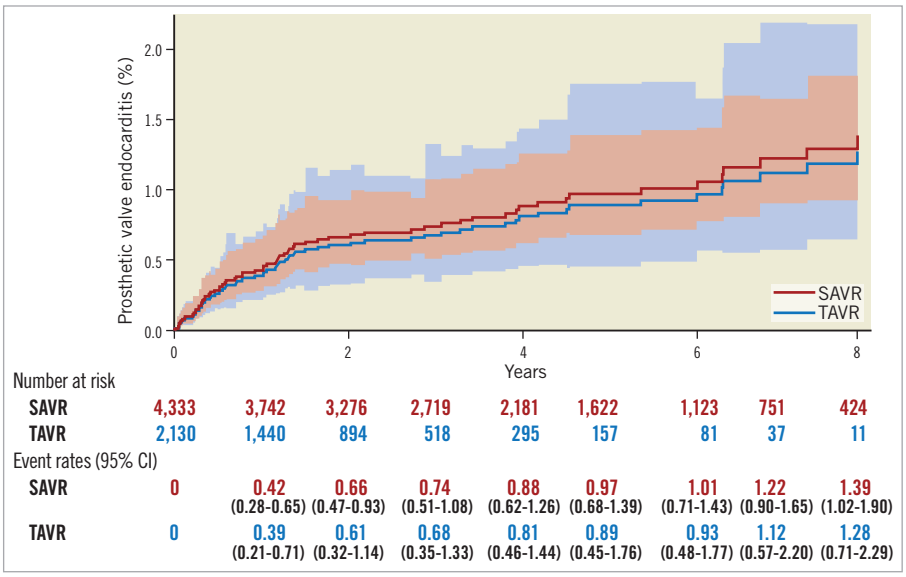
The main clinical features of PVE are shown in **Table 2**. Among 68 patients with PVE, staphylococci were the most frequent causal microorganisms (38.2%). Surgical treatment was less frequently performed in the TAVR cohort compared with the SAVR cohort (6.7% vs 47.2%, p=0.004). In-hospital death occurred in 19 patients (27.9%). The detailed individual data of patients with PVE are reported in **Supplementary Table 3**. Surgical treatment for PVE was the only independent predictor of in-hospital death (HR 0.34, 95% CI: 0.21-0.61) **(Figure 3)**. The mortality rate after PVE was 37.7% at one month and 52.5% at 12 months **(Figure 4)**.

Discussion

The FinnValve registry showed that there was no difference in the risk of PVE after TAVR and SAVR over time. We also observed that the incidence of PVE was significantly associated with male gender and DSWI or vascular access-site infection following AVR. Furthermore, an excessive rate of mortality was observed in patients who developed PVE.

The incidence of PVE after SAVR is well estimated, ranging from 3 to 12/1,000 person-years[6], similar to the overall incidence of 3.0/1,000 person-years observed in this study. With regard to TAVR, the incidence of PVE has been reported to be between 0.3% and 3.4% at one-year follow-up[4,23-26]. In the PARTNER trial, PVE at five years occurred in 2.0% of patients with TAVR[27]. Currently, the data on PVE beyond five years are scarce. In this study, we used a competing risk method to elucidate the risk of PVE as suggested by a consensus statement[1]. Indeed, in this context the Kaplan-Meier method censors patients who die before the occurrence of PVE; this may lead to an overestimation of the risk of PVE[21,28,29]. Using the competing risk regression method, we observed that the risk of PVE was similar after TAVR and SAVR.

Our study showed an independent association between the development of PVE and male gender. A meta-analysis suggested that native valve endocarditis occurs more frequently in males[30]. Østergaard et al reported that PVE is also more common



Number at risk									
SAVR	4,333	3,742	3,276	2,719	2,181	1,622	1,123	751	424
TAVR	2,130	1,440	894	518	295	157	81	37	11
Event rates (95% CI)									
SAVR	0	0.42 (0.28-0.65)	0.66 (0.47-0.93)	0.74 (0.51-1.08)	0.88 (0.62-1.26)	0.97 (0.68-1.39)	1.01 (0.71-1.43)	1.22 (0.90-1.65)	1.39 (1.02-1.90)
TAVR	0	0.39 (0.21-0.71)	0.61 (0.32-1.14)	0.68 (0.35-1.33)	0.81 (0.46-1.44)	0.89 (0.45-1.76)	0.93 (0.48-1.77)	1.12 (0.57-2.20)	1.28 (0.71-2.29)

Figure 1. *The risk in competing risk analysis with the occurrence of prosthetic valve endocarditis after TAVR and SAVR. There was no significant difference in the risk of PVE between TAVR and SAVR over an eight-year period. CI: confidence interval; SAVR: surgical aortic valve replacement; TAVR: transcatheter aortic valve replacement*

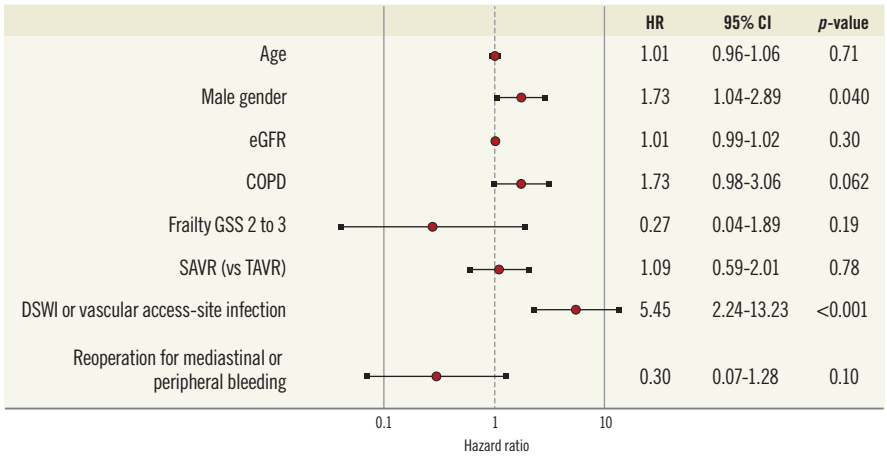


Figure 2. *Factors associated with the incidence of prosthetic valve endocarditis following aortic valve replacement with a bioprosthesis. Multivariate analysis including patients' baseline covariates and early adverse events. CI: confidence interval; COPD: chronic obstructive pulmonary disease; DSWI: deep sternal wound infection; eGFR: estimated glomerular filtration rate; GSS: geriatric status scale; SAVR: surgical aortic valve replacement; TAVR: transcatheter aortic valve replacement*

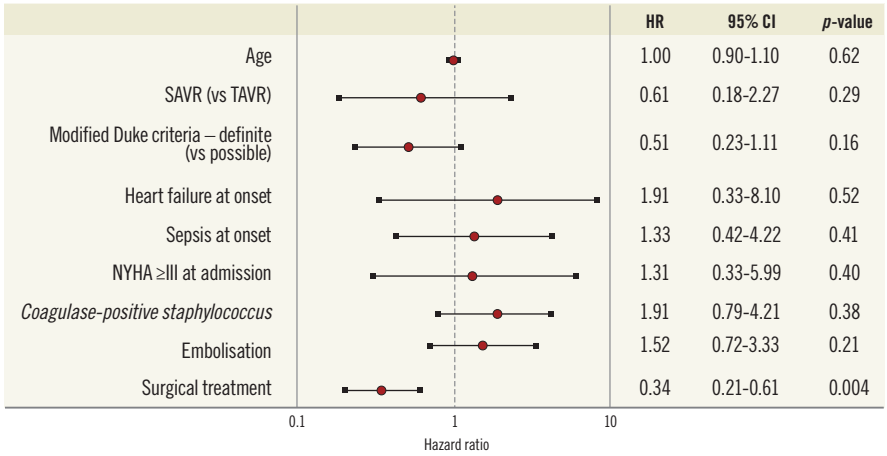


Figure 3. *Factors associated with in-hospital mortality following prosthetic valve endocarditis. Multivariate analysis including age at the time of PVE diagnosis and clinical features of patients with PVE. CI: confidence interval; NYHA: New York Heart Association; SAVR: surgical aortic valve replacement; TAVR: transcatheter aortic valve replacement*

in males[31]. These reports support a gender difference regarding the risk of PVE. The potential mechanism of less frequent PVE in females could be partially explained by endothelial protection by oestrogen release[32]. Furthermore, DSWI or vascular access-site infection was significantly associated with an increased risk of PVE. El-Ahdab et al reported that bacteraemia after AVR is highly associated with an increased risk of PVE[33]. Since surgical and vascular access-site infection are the possible causes of bacteraemia leading to PVE, a strategy of prolonged antibiotic therapy may be indicated in such patients.

PVE is a critical condition, with a risk of in-hospital mortality of 23% to 40%[34-36]. Patients with PVE due to coagulase-positive staphylococcus revealed more severe conditions than those with PVE due to other organisms **(Supplementary Table 4)**. However, surgical treatment was only associated with significantly decreased in-hospital mortality. Nevertheless, the rate of surgical treatment was very low in the TAVR group in the current study. We should acknowledge that only surgical treatment can improve the prognosis of patients with PVE despite the high surgical risk.

Limitations

Our study has several limitations, mainly related to its retrospective nature. Second, the diagnosis of PVE has been well validated by several experienced cardiologists and cardiac surgeons. However, there was no external monitoring committee to verify the accuracy of the data reported by each centre. This may have led to underestimation of the incidence of PVE. Finally, the influence of unknown confounding factors other than those included in the multivariate model for the incidence of PVE cannot be ruled out.

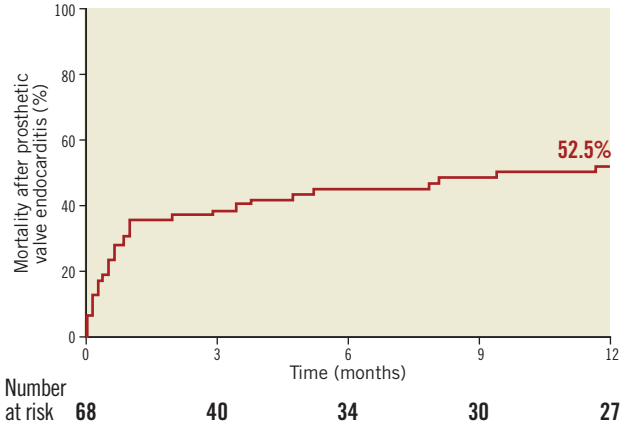


Figure 4. *Kaplan-Meier estimate of mortality at 12-month follow-up in patients with prosthetic valve endocarditis. The mortality rate is 37.7% at one month and 52.5% at 12 months.*

Conclusions

The risk of PVE after TAVR is similar to that following SAVR over time. Patients who develop PVE have a high rate of mortality. These results may have clinical impact on our decision making when we consider expanding the indication of TAVR to low-risk, especially younger populations. Further studies are needed to improve the management of such a critical complication.

Impact on daily practice

In patients who underwent aortic valve replacement, PVE is very rare. Durability of TAVR in terms of PVE is similar to SAVR with a bioprosthesis over time. Prosthetic valve endocarditis is associated with a high rate of mortality. Further studies are needed to improve the prognosis of patients who have PVE after aortic valve replacement.

Conflict of interest statement

The authors have no conflicts of interest to declare.

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Supplementary data

Supplementary Appendix 1. Propensity score matching.

Supplementary Figure 1. Study flow chart.

Supplementary Figure 2. The risk in competing risk analysis with the occurrence of prosthetic valve endocarditis after TAVR and SAVR in a propensity-matched cohort.

Supplementary Table 1. Inclusion and exclusion criteria.

Supplementary Table 2. Baseline characteristics and rates of prosthesis valve endocarditis in patients who underwent TAVR or SAVR in the unmatched and propensity-matched cohorts.

Supplementary Table 3. Individual data of patients with prosthetic valve endocarditis after aortic valve replacement.

Supplementary Table 4. Clinical characteristics and outcomes of prosthetic valve endocarditis according to the microorganisms.

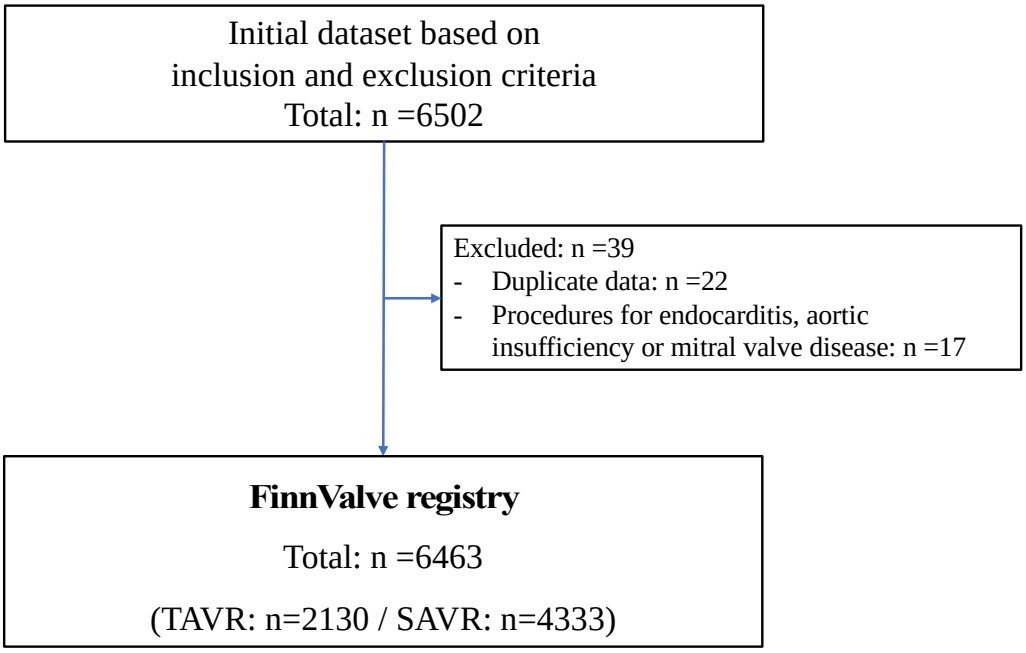
The supplementary data are published online at: https://eurointervention.pcronline.com/doi/10.4244/EIJ-D-19-00247

Supplementary data

Supplementary Appendix 1. Propensity score matching

A propensity score was estimated using a non-parsimonious logistic regression model including all the covariates listed in Table 1. One-to-one propensity score matching was performed employing the nearest neighbour method and a calliper width of 0.2 of the standard deviation of the logit of the propensity score. One-to-one propensity score matching was performed and, to evaluate the balance between the matched groups, the analysis of the standardised differences after matching was used. Standardised differences lower than 0.10 were considered an acceptable imbalance between the treatment groups.

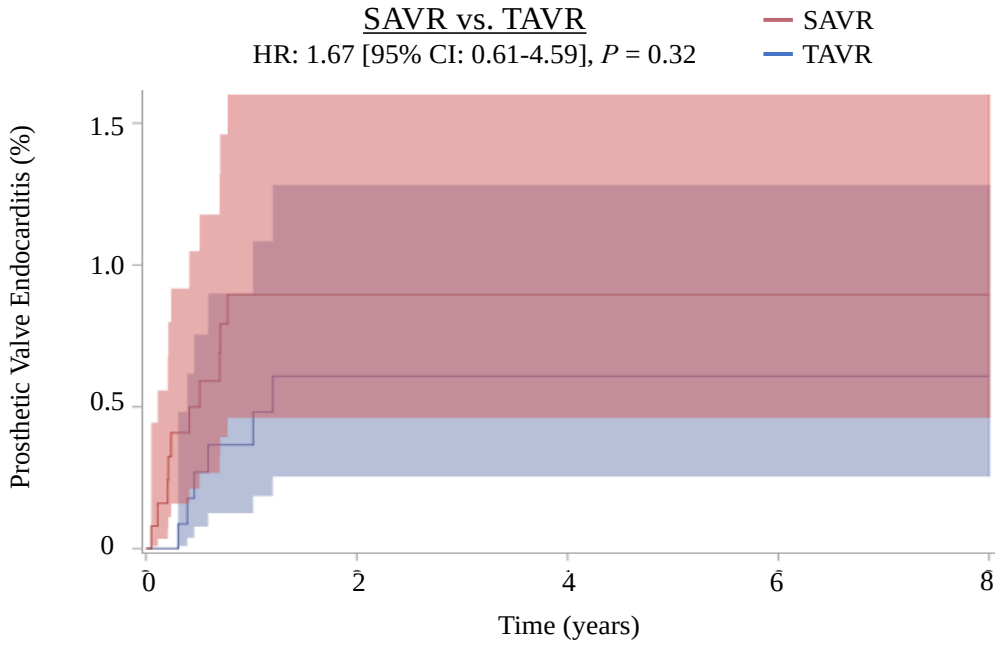
A non-parsimonious logistic regression model included the following covariates: age, gender, body mass index, haemoglobin, eGFR, dialysis, diabetes, chronic obstructive pulmonary disease, atrial fibrillation, extracardiac arteriopathy, active malignancy, Frailty GSS 2 to 3, prior cardiac surgery, prior pacemaker implantation, prior PCI, critical operative state, NYHA Class Ⅳ, LVEF <51%, bicuspid aortic valve, coronary artery disease, urgent/emergent procedure, EuroSCORE II and STS score.



Supplementary Figure 1. Study flow chart.

The FinnValve registry includes 6,463 patients who underwent primary TAVR or SAVR with a bioprosthesis for severe aortic stenosis.

SAVR: surgical aortic valve replacement; TAVR: transcatheter aortic valve replacement



Supplementary Figure 2. The risk in competing risk analysis with the occurrence of prosthetic valve endocarditis after TAVR and SAVR in the propensity-matched cohort. Cumulative incidence of prosthetic valve endocarditis (PVE) adjusting for the competing risk of death. There was no significant difference in the risk of PVE between TAVR and SAVR (HR 1.67, 95% CI: 0.61-4.59 for SAVR). Curves are reported with 95% CI.

CI: confidence interval; HR: hazard ratio; SAVR: surgical aortic valve replacement; TAVR: transcatheter aortic valve replacement

Supplementary Table 1. Inclusion and exclusion criteria.

Inclusion criteria:

1) age >18 years; 2) primary aortic valve procedure with a bioprosthesis for AS with or without aortic valve regurgitation; or 3) TAVR or SAVR with or without associated coronary revascularisation.

Exclusion criteria:

1) any prior TAVR or surgical intervention on the aortic valve; 2) concomitant major procedure on the mitral valve, tricuspid valve and/or ascending aorta; 3) any procedure for isolated aortic valve regurgitation; or 4) active endocarditis.

Clinical Trial Registration: ClinicalTrials.gov Identifier: NCT03385915.

URL https://clinicaltrials.gov/ct2/show/NCT03385915

Supplementary Table 2. Baseline characteristics and rates of prosthesis valve endocarditis in patients who underwent TAVR or SAVR in the unmatched and propensity-matched cohorts.

	Unmatched cohort			**Propensity score matched cohort**		
Baseline characteristics	TAVR (n=2,130)	SAVR (n=4,333)	Standardised differences	TAVR (n=1,252)	SAVR (n=1,252)	Standardised differences
Age, yrs	81.2±6.6	75.1±6.5	0.939	79.6±7.0	80.2±4.5	0.099
Female, n	1,172 (55.0)	2,026 (46.8)	0.166	712 (56.9)	747 (59.7)	0.057
Body mass index, kg/m^2	27.1±4.8	27.7±4.8	0.115	274±5.1	27.4±4.7	0.005
Haemoglobin, g/l	125±16	132±15	0.481	127±16	125±14	0.088
eGFR, ml/min/1.73 m^2	65±23	76±21	0.465	69±23	68±20	0.055
Dialysis, n	24 (1.1)	14 (0.3)	0.094	7 (0.6)	8 (0.6)	0.010
Diabetes, n	605 (28.4)	1,154 (26.6)	0.040	341 (27.2)	355 (28.4)	0.025
COPD, n	456 (21.4)	642 (14.8)	0.172	240 (19.2)	266 (21.2)	0.052
Atrial fibrillation, n	932 (43.8)	955 (22.0)	0.475	439 (35.1)	473 (37.8)	0.056
Extracardiac arteriopathy, n	412 (19.3)	539 (12.4)	0.190	207 (16.5)	226 (18.1)	0.040
Coronary artery disease, n	603 (28.3)	1,970 (45.5)	0.361	419 (33.5)	363 (29.0)	0.097
Active malignancy, n	84 (3.9)	60 (1.4)	0.159	30 (2.4)	33 (2.6)	0.015
Prior pacemaker implant., n	208 (9.8)	174 (4.0)	0.228	76 (6.1)	91 (7.3)	0.048
Prior cardiac surgery, n	431 (20.2)	97 (2.2)	0.594	88 (7.0)	85 (6.8)	0.009
Prior PCI, n	467 (21.9)	405 (9.3)	0.351	200 (16.0)	198 (15.8)	0.004
Frailty GSS ≥2, n	318 (14.9)	107 (2.5)	0.453	94 (7.5)	91 (7.3)	0.009
Critical preoperative state, n	48 (2.3)	113 (2.6)	0.023	29 (2.3)	31 (2.5)	0.010
NYHA class IV, n	244 (11.5)	453 (10.5)	0.032	135 (10.8)	136 (10.9)	0.003
LVEF ≤50%, n	596 (28.0)	909 (21.0)	0.164	303 (24.2)	305 (24.4)	0.004
Bicuspid aortic valve, n	114 (5.4)	920 (21.2)	0.481	89 (7.1)	63 (5.0)	0.087
Urgent or emergent procedure, n	158 (7.4)	588 (13.6)	0.202	112 (8.9)	104 (8.3)	0.023
EuroSCORE II, %	7.2±7.4	4.2±5.5	0.464	5.4±5.6	5.6±6.6	0.020
STS score, %	4.6±3.3	3.1±2.9	0.502	3.9±2.6	4.1±3.7	0.050

	TAVR	SAVR	*p*-value	TAVR	SAVR	*p*-value
Prosthetic valve endocarditis, rates			0.449			0.318
1-year	0.5%	0.5%		0.4%	0.9%	
2-year	0.8%	0.8%		0.6%	0.9%	
4-year	0.9%	1.1%		0.6%	0.9%	
6-year	0.9%	1.3%		0.6%	0.9%	
8-year	0.9%	1.8%		0.6%	0.9%	

Values are expressed as counts and percentages (in parentheses) or as mean and standard deviation (in parentheses).

COPD: chronic obstructive pulmonary disease; eGFR: estimated glomerular filtration rate; GSS: geriatric status scale; LVEF: left ventricular ejection fraction; NYHA: New York Heart Association; PCI: percutaneous coronary intervention; SAVR: surgical aortic valve replacement; STS: Society of Thoracic Surgeons; TAVR: transcatheter aortic valve replacement

Supplementary Table 3. Individual data of patients with prosthetic valve endocarditis after aortic valve replacement.

No.	Age / gender	Type of AVR/PV	Time from AVR (days)	Time from onset to diagnosis (days)	Modified Duke criteria*	Microorganism(s) found in blood culture	Echocardiographic findings	Embolism	Antibiotic	Additional invasive treatment	In-hospital death	Death / time from PVE (days)
1	71 / male	SAVR / Epic	30	5	Definite (M:2; m:1,3,5)	*Staphylococcus aureus*	Vegetation, PVL	Brain	Ceftriaxone	Bentall procedure	Yes	Yes / 7
2	66 / female	SAVR / Epic	1,387	4	Definite (M:1,2; m:1,2)	*Enterococcus faecalis*	Vegetation	No	Ceftriaxone	No	Yes	Yes / 18
3	75 / female	SAVR / Soprano	3,314	52	Definite (M:1,2; m:1,2)	*Streptococcus viridans*	Leaflet dehiscence, pseudoaneurysm	No	Vancomycin, Penicillin	SAVR	No	No
4	83 / male	SAVR / Mitroflow	639	7	Definite (M:1; m:1,2,3,4)	*Staphylococcus aureus*	Annular abscess	Brain	Imipenem, Tazobactam	No	Yes	Yes / 4
5	72 / male	SAVR / Epic	18	1	Definite (M:1,2; m:1,2)	*Staphylococcus epidermidis*	Prosthetic valve regurgitation	No	Vancomycin, Rifampicin	No	No	No
6	79 / male	SAVR / Epic	497	23	Definite (M:2; m:1,2,3)	Unknown	Vegetation, PVL	Brain, spleen	Tobramycin	SAVR	No	No
7	78 / male	SAVR / Mitroflow	285	63	Definite (M:1,2;	*Enterococcus faecalis*	Vegetation, annular abscess	Brain, spleen	Vancomycin, Ampicillin	SAVR	No	No

					m:1,2,3)							
8	68 / male	SAVR / Soprano	993	259	Definite (M:1,2; m:1,2,3)	*Streptococcus agalactiae*	Vegetation, annular abscess, fistula	No	Cefuroxime	SAVR with reconstruction of the aortic annulus and suture of fistula	Yes	Yes / 7
9	69 / male	SAVR / Freedom Solo	1,431	9	Definite (M:1,2; m:1,2)	*Enterococcus faecalis*	Vegetation, annular abscess	No	Levofloxacin	Bentall procedure	Yes	Yes / 26
10	83 / male	SAVR / Mitroflow	124	250	Definite (M:2; m:1,2,3)	*Staphylococcus warneri*	No	Spine	Cefuroxime	No	No	No
11	82 / male	SAVR / Mitroflow	464	44	Definite (M:1,2; m:1,2,3)	*Enterococcus faecalis*	Vegetation, annular abscess	Brain, spleen	Imipenem	No	Yes	Yes / 285
12	68 / male	SAVR / Hancock Ultra II	2,654	32	Definite (M:2; m:1,2,5)	*Serratia marcescens*	Vegetation	No	Meropenem	No	No	Yes / 157
13	68 / male	SAVR / Mitroflow	383	11	Definite (M;1,2; m:1,2)	*Streptococcus pneumoniae*	Vegetation, leaflet dehiscence	No	Ciprofloxacin, Ceftriaxone, Penicillin	SAVR	No	No
14	84 / female	SAVR /	2,862	24	Possible	*Streptococcus*	Suspected	No	Ceftriaxone,	No	No	No

		Mitroflow			(M:1; m:1)	*viridans*	vegetation		Penicillin			
15	86 / female	TAVR / SAPIEN XT	128	1	Definite (M:1,2; m:1,2)	*Enterococcus faecalis*	Vegetation, prosthetic valve regurgitation	No	Ampicillin, Vancomycin, Tobramycin	No	No	Yes / 102
16	83 / male	TAVR / CoreValve	372	3	Definite (M:1,2; m:1,2)	*Staphylococcus aureus*	Prosthetic valve regurgitation	No	Cefuroxime, Piperacillin-tazobactam	No	No	Yes / 59
17	70 / male	SAVR / Mitroflow	1,442	2	Definite (M:1,2; m:1,3)	*Enterococcus faecalis*	Vegetation, annular abscess	Brain	Ceftriaxone, Gentamicin, Vancomycin	SAVR	No	No
18	76 / female	TAVR / PERIMOUNT Magna Ease	336	53	Definite (M:1,2; m:1,2,3)	*Streptococcus pyogenes, streptococcus agalactiae*	Vegetation, leaflet dehiscence, prosthetic valve regurgitation	Spine	Penicillin, Tobramycin	No	Yes	Yes / 30
19	70 / female	SAVR / Mitroflow	3,472	274	Definite (M:1,2; m:1,2,3)	*Staphylococcus epidermidis*	Vegetation	No	Cloxacillin, Tobramycin	No	No	Yes / 19
20	87 / female	TAVR / SAPIEN 3	285	2	Definite (M:1,2; m:1)	*Streptococcus viridans*	Vegetation	No	Penicillin	No	No	Yes / 580
21	80 / male	SAVR / Hancock Ultra	256	29	Definite (M:2; m:1,2,5)	*Staphylococcus epidermis*	Vegetation, annular abscess	No	Daptomycin, Linezolid	Bentall procedure	Yes	Yes / 1

		II										
22	69 / male	SAVR / Epic	33	8	Possible (M:1; m:1,2)	*Propionibacterium acnes*	Prosthetic valve regurgitation	No	Meropenem, Vancomycin	SAVR	No	No
23	89 / male	SAVR / Epic	187	8	Definite (M:1,2; m:1)	*Staphylococcus epidermidis*	Vegetation, annular abscess	No	Gentamicin, Rifampicin, Vancomycin	SAVR	No	No
24	62 / female	SAVR / Freedom Solo	1,526	1	Definite (M:1,2; m:1,2,3)	*Staphylococcus aureus*	Vegetation, annular abscess, fistula	No	Cefuroxime, Piperacillin-tazobactam	SAVR	Yes	Yes / 26
25	68 / male	SAVR / Hancock Ultra II	2,296	195	Possible (m:1,3,4)	*Bartonella quintana*	No	Brain	Moxifloxacin	SAVR	No	Yes / 814
26	69 / male	SAVR / Mosaic Ultra	1,654	20	Definite (M:1,2; m:1,2)	*Enterococcus faecalis*	Vegetation	No	Ampicillin	No	No	No
27	61 / male	SAVR / Mosaic Ultra	2,453	40	Possible (M:2; m:1,2)	*Unknown*	Vegetation	No	Linezolid, Meropenem	No	No	Yes / 245
28	79 / male	SAVR / Soprano	428	284	Possible (M:2; m:1,5)	*Unknown*	Prosthetic valve regurgitation	No	Imipenem, Levofloxacin, Vancomycin	SAVR	No	Yes / 942
29	83 / female	SAVR / Mitroflow	77	196	Definite (M:1,2; m:1,2)	*Staphylococcus epidermidis*	Annular abscess, leaflet dehiscence	No	Ciprofloxacin, Vancomycin	SAVR	No	No

30	70 / male	SAVR / Trifecta	796	3	Definite (M:2; m:1,2,3)	*Streptococcus angiosus*	Vegetation	Brain	-	No	Yes	Yes / 1
31	76 / female	SAVR / Crown	420	4	Definite (M:1,2; m:1,2)	*Streptococcus mitis*	Vegetation, prosthetic valve regurgitation	No	Cefuroxime	No	Yes	Yes / 1
32	71 / male	SAVR / PERIMOUNT Magna Ease	110	7	Definite (M:1; m:1,2,3)	*Candida albicans*	Vegetation, annular abscess	Lower limb	Fluconazole	No	No	Yes / 143
33	80 / female	SAVR / Epic	201	7	Definite (M:1,2; m:1,2)	*Enterococcus faecalis*	Vegetation	No	Cloxacillin, Rifampicin	No	No	Yes / 1,249
34	91 / male	TAVR / Lotus	734	1	Possible (M:1; m:1,2)	*Enterococcus faecalis*	No	No	Ampicillin	No	No	No
35	71 / male	SAVR / Epic	4	96	Possible (M:2, m:1,2)	*Unknown*	Leaflet dehiscence	No	Cefroxime, Vancomycin	SAVR+ repair of the ascending aorta	No	Yes / 1,252
36	76 / female	SAVR / Epic	117	50	Definite (M:1,2; m:1)	*Staphylococcus epidermidis*	Vegetation	No	Ampicillin, Gentamicin	No	No	No
37	70 / male	SAVR / Epic Supra	103	248	Definite (M:2; m:1,2,5)	*Staphylococcus capitis*	Annular abscess, leaflet dehiscence	No	Ceftriaxone, Vancomycin	Bentall procedure	No	No
38	91 / female	TAVR /	216	10	Definite	*Group G β-*	No	No	Amoxicillin,	No	No	Yes / 1,263

		SAPIEN XT			(M:1; m:1,2,5)	*haemolytic streptococci*			Ceftriaxone, Vancomycin			
39	81 / male	TAVR / SAPIEN 3	504	252	Definite (M:1,2; m:1,2)	*Streptococcus viridans*	Vegetation	No	Penicillin, Tazobactam	No	No	No
40	65 / male	SAVR / PERIMOUNT Magna Ease	603	23	Possible (M:2; m:1,5)	*Streptococcus intermedius*	Vegetation	No	Penicillin, Cefuroxime	No	No	No
41	73 / female	SAVR / PERIMOUNT Magna Ease	1,117	14	Definite (M:1,2; m:1,2,3)	*Staphylococcus aureus*	Vegetation, annular abscess	Brain, spine	Ampicillin, Rifampicin	No	No	No
42	85 / male	SAVR / Mitroflow	88	30	Possible (M:1; m:1,2)	*Staphylococcus epidermidis*	No	No	Ceftriaxone, Vancomycin	No	No	Yes / 19
43	90 / female	TAVR / SAPIEN 3	103	42	Definite (M:1,2; m:1,2)	*Streptococcus sanguinis*	Vegetation	No	Ceftriaxone, Unknown	No	No	No
44	70 / male	SAVR / Epic	369	36	Definite (M:1,2, m:1,2)	*Staphylococcus aureus, Staphylococcus epidermidis*	Vegetation, annular abscess	No	Ampicillin, Vancomycin	SAVR	No	Yes / 2,194
45	85 / male	SAVR / Mitroflow	150	253	Definite (M:1,2; m:1,2)	*Staphylococcus epidermidis*	Fistula	No	Piperacillin-tazobactam, Vancomycin	No	Yes	Yes / 7

46	51 / male	SAVR / Trifecta	479	27	Definite (M:1,2; m:1,2)	*Staphylococcus epidermidis*	Vegetation	No	Ampicillin, Rifampicin	No	Yes	Yes / 1
47	90 / female	TAVR / Lotus	435	7	Definite (M:1,2; m:1,2)	*Enterococcus faecalis*	Vegetation	No	Cefuroxime	No	No	No
48	70 / male	SAVR / Trifecta	475	29	Definite (M:1,2; m:1,2,3)	*Streptococcus viridans*	Vegetation, annular abscess	No	Penicillin, Vancomycin	SAVR	No	Yes / 1,183
49	78 / male	SAVR / Trifecta	190	2	Definite (M:1,2; m:1,5)	*Staphylococcus warneri*	Vegetation	No	Vancomycin, Moxifloxacin	No	No	Yes / 114
50	72 / female	SAVR / Mitroflow	1,048	4	Definite (M:1,2; m:1,2,3)	*Staphylococcus aureus*	No	Brain	Gentamicin, Vancomycin	No	Yes	Yes / 3
51	79 / male	SAVR / Mitroflow	2,230	51	Definite (M:1, m:1,2,3)	*Staphylococcus epidermidis*	No	No	Daptomycin, Rifampicin	No	Yes	Yes / 11
52	68 / male	TAVR / Lotus	110	20	Definite (M:1,2; m:1,2)	*Enterococcus faecalis*	No	No	Cefuroxime	No	No	No
53	85 / female	TAVR / Evolut R	212	19	Possible (m:1,2,5)	*Streptococcus oralis*	No	No	Cefroxime	No	No	No
54	69 / female	SAVR / Epic	1,249	258	Definite (M:1,2; m:1,2,3)	*Enterococcus faecalis*	Vegetation	No	Unknown	No	No	No

55	80 / male	SAVR / Mitroflow	2,190	4	Definite (M:1,2; m:1.2)	*Enterococcus faecalis*	Vegetation, annular abscess	No	Ampicillin, Gentamicin	No	No	Yes / 355
56	91 / male	TAVR / Lotus	26	2	Definite (M:1,2; m:1,2,4)	*Staphylococcus aureus*	Vegetation	No	Ceftriaxone, Vancomycin	No	Yes	Yes / 15
57	75 / male	Hancock Ultra II	1,643	23	Definite (M:1,2; m:1)	*Citrobacter diversus*	Suspected vegetation	No	Penicillin	No	No	Yes / 238
58	79 / female	SAVR / Trifecta	88	3	Definite (M:1,2; m:1,2,3)	*Unknown*	Leaflet dehiscence	No	Tazobactam, Rifampicin, Vancomycin	SAVR	No	No
59	86 / female	SAVR / Mitroflow	41	39	Definite (M:1,2; m:1,2,3)	*Staphylococcus epidermidis*	Vegetation, annular abscess	Brain	Penicillin, Vancomycin	SAVR	Yes	Yes / 15
60	72 / male	SAVR / PERIMOUNT Magna Ease	15	39	Definite (M:1,2; m:1,2,3)	*Staphylococcus aureus*	Vegetation	No	Cloxacillin, Rifampicin	No	No	Yes / 15
61	69 / female	SAVR / Mitroflow	1,957	13	Definite (M:1; m:1,2,4,5)	*Streptococcus viridans*	No	No	Ceftriaxone	No	No	Yes / 33
62	91 / female	TAVR / SAPIEN XT	544	19	Definite (M:1,2;	*Streptococcus viridans*	Vegetation	Brain	Cephalosporin, Vancomycin	No	No	Yes / 88

					m:1,2,3)							
63	60 / male	TAVR / Evolut R	380	211	Possible (M:1; m:1,2)	*Streptococcus viridans*	No	No	Ampicillin, Vancomycin	SAVR	No	No
64	81 / female	TAVR / SAPIEN 3	438	4	Definite (M:1,2; m:1,2)	*Staphylococcus epidermidis*	New prosthetic valve regurgitation	No	Ceftriaxone, Vancomycin	No	Yes	Yes / 2
65	76 / male	SAVR / Mitroflow	77	20	Definite (M:1; m:1,2,3)	*Streptococcus viridans*	No	Brain	Ceftriaxone, Vancomycin	No	Yes	Yes / 1
66	74 / male	SAVR / Mitroflow	256	35	Definite (M:1,2; m:1,2,3)	*Streptococcus viridans*	Vegetation, pseudoaneurysm	Spine	Ciprofloxacin, Penicillin, Tobramycin	SAVR	No	No
67	76 / male	SAVR / PERIMOUNT Magna Ease	1,201	38	Definite (M:1,2; m:1,2)	*Staphylococcus aureus*	Vegetation, annular abscess	Spleen	Penicillin, Moxifloxacin	SAVR	No	Yes / 30
68	83 / female	TAVR / SAPIEN XT	143	1	Definite (M:1; m) (Diagnosed by autopsy)	*Staphylococcus aureus*	No (Vegetation found by autopsy)	No	Penicillin, Vancomycin	No	Yes	Yes / 1

AVR: aortic valve replacement; PV: prosthetic valve; PVE: prosthetic valve endocarditis; SAVR: surgical aortic valve replacement; TAVR: transcatheter aortic valve replacement

*Description of the Modified Duke criteria - Definite infective endocarditis: 2 major criteria OR 1 major criterion + 3 minor criteria; OR 5 minor criteria. Possible infective endocarditis: 1 major criterion + 1 minor criterion OR 3 minor criteria.

M: major criteria; m: minor criteria.

M1: positive blood culture for typical infective endocarditis organisms from 2 separate blood cultures or 2 positive cultures from samples drawn >12 hours apart, or 3 or a majority of 4 separate cultures of blood; M2: echocardiographic findings supporting endocarditis; M3: single positive blood culture for *Coxiella burnetii* or anti-phase 1 IgG antibody titer >1:800; m1: predisposing heart condition or intravenous drug use; m2: temp >38 degrees C; m3: vascular phenomena; m4: immunologic phenomena; m5: other microbiological evidence

Supplementary Table 4. Clinical characteristics and outcomes of prosthetic valve endocarditis according to the microorganisms.

	Coagulase-positive staphylococcus (n=11)	*Coagulase-negative staphylococcus* (n=15)	*Enterococci* (n=13)	*Streptococci* (n=19)	*Others*[*] (n=10)	*p*-value
Time from indexed AVR, yrs	1.6±1.5	1.5±2.7	2.5±1.9	2.1±2.5	2.8±3.0	0.63
First symptom						
Fever	7 (63.6)	11 (73.3)	9 (69.2)	17 (89.5)	5 (50)	0.22
Sepsis	6 (54.6)	4 (26.7)	3 (23.1)	3 (15.8)	2 (20.0)	0.21
Heart failure	1 (9.1)	2 (13.3)	1 (7.7)	2 (10.5)	1 (10.0)	0.99
Bradycardia	0 (0)	1 (6.7)	1 (7.7)	2 (10.5)	0 (0)	0.71
Neurological	0 (0)	0 (0)	0 (0)	2 (10.5)	0 (0)	0.26
Weight loss	0 (0)	0 (0)	0 (0)	0 (0)	2 (20.0)	0.018
Onset to diagnosis, days						
Mean	13.6±15.9	97.4±109.6	33.7±70.0	56.9±83.5	71.1±95.0	0.11
Median	5 (2-36)	39 (8-248)	7 (3-32)	23 (11-52)	28 (8-121)	-
Modified Duke criteria, definite	11 (100)	14 (93.3)	12 (93.3)	15 (79.0)	5 (50.0)	0.014
Echocardiographic finding(s)	9 (81.8)	11 (73.3)	11 (84.6)	14 (73.7)	10 (100)	0.45
Vegetation	7 (63.6)	7 (46.7)	11 (84.6)	10 (52.6)	5 (50.0)	0.27
Abscess	5 (45.5)	5 (33.3)	4 (30.8)	2 (10.5)	1 (10.0)	0.16
Leaflet dehiscence	0 (0)	2 (13.3)	0 (0)	2 (10.5)	2 (20.0)	0.36
Fistula	1 (9.1)	1 (6.7)	0 (0)	2 (10.5)	0 (0)	0.66
Pseudoaneurysm	0 (0)	0 (0)	0 (0)	2 (10.5)	0 (0)	0.26
Embolisation	5 (45.5)	2 (13.3)	3 (23.1)	5 (26.3)	3 (30.0)	0.48
In-hospital death	6 (54.6)	6 (40.0)	3 (23.1)	5 (26.3)	0 (0)	0.035

Values are expressed as n (%), mean ± standard deviation (SD), or median (IQR 25-75%).

[*]Others = including fungal and blood culture negative infective endocarditis (BCNIE).

AVR: aortic valve replacement