Surgical results for prosthetic versus native valve endocarditis: A multicenter analysis

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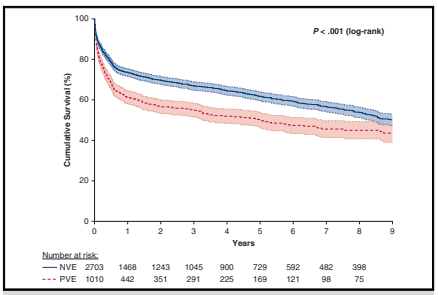
ABSTRACT

Objectives: Prosthetic valve endocarditis is associated with worse outcomes compared with native valve endocarditis. Our aim was to evaluate the impact of native valve endocarditis versus prosthetic valve endocarditis on postoperative outcomes and long-term survival and to identify preoperative risk factors in a large cohort of 4300 patients with infective endocarditis.

Methods: This retrospective cohort study was conducted in 5 German Cardiac Surgery Centers: the Clinical Multicenter Project of Analysis of Infective Endocarditis in Germany. Data of 4300 patients undergoing valve surgery for native valve endocarditis and prosthetic valve endocarditis were retrospectively analyzed. Univariable and multivariable analyses were used for risk stratification, Kaplan–Meier analysis for long-term survival. In addition, we performed Cox proportional hazards regression with multivariable adjustment.

Results: Between 1994 and 2016, 3143 patients (73.1%) underwent surgery for native valve endocarditis and 1157 patients (26.9%) underwent surgery for prosthetic valve endocarditis. Patients with prosthetic valve endocarditis were older (69 [60-75] vs 63 [52-72] years; $P < .001$) and had more comorbidities, such as hypertension (55% vs 46%; $P < .001$), diabetes (28% vs 25%; $P = .020$), coronary artery disease (32% vs 23%; $P < .001$), and preoperative acute kidney injury (41% vs 32%; $P < .001$). Kaplan–Meier analysis revealed significantly decreased long-term survival of patients undergoing surgery for prosthetic valve endocarditis compared with native valve endocarditis ($P < .001$). However, after multivariable adjustment, there was no significant difference in long-term survival between patients undergoing cardiac surgery with prosthetic valve endocarditis compared with native valve endocarditis.

Conclusions: After adjusting for preoperative comorbidities, long-term survival for prosthetic valve endocarditis and native valve endocarditis is comparable. Thus, our large cohort study provides evidence that prosthetic valve endocarditis alone should not be a contraindication for redo operations. (J Thorac Cardiovasc Surg 2021;161:609-19)



Significantly decreased long-term survival of patients with PVE compared with NVE.

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CENTRAL MESSAGE

Early and late mortality remain high in patients undergoing surgery for PVE. After adjusting for preoperative comorbidities, long-term survival for PVE and NVE is comparable.

PERSPECTIVE

Information on long-term prognosis of patients undergoing surgery for PVE is scarce and limited by small sample size or single-center experiences. Our multicenter retrospective analysis provides evidence that although PVE is associated with high mortality rates, long-term survival is comparable to NVE. Thus, diagnosis of PVE should not hinder surgeons from pursuing cardiac surgery.

See Commentaries on pages 620 and 622.

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Abbreviations and Acronyms

AKI	= acute kidney injury
CPB	= cardiopulmonary bypass
euroSCORE	= European System for Cardiac Operative Risk Evaluation
IE	= infective endocarditis
IQR	= interquartile range
MVA	= multivariable analysis
NVE	= native valve endocarditis
PVE	= prosthetic valve endocarditis

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Prosthetic valve endocarditis (PVE) is a serious complication of valve replacement, reported to occur with an incidence of 0.3% to 1.2% per patient-year, corresponding to 3% to 6% of all patients receiving a prosthetic valve within 5 years of implantation.[1-3] The clinical characteristics of patients undergoing surgery for PVE are gaining interest because of the increasing population with prosthetic valves or nosocomial infections.[4] Compared with native valve endocarditis (NVE), PVE remains a serious condition with a considerable higher in-hospital mortality of 19% to 50% versus 7% to 13% in patients with NVE.[4-6]

Despite improvements in prophylactic, diagnostic, and therapeutic strategies, neither the incidence nor the mortality of infective endocarditis (IE) has been reduced in the past 30 years.[7,8] Numerous studies have attempted to identify risk factors predictive of early and late mortality.[3,9-13] Most important adverse prognostic factors were PVE,[14] *Staphylococcus aureus* infection,[2,13,14] increased age,[1,2,13] and renal insufficiency.[1,15]

However, much of the current understanding of PVE has been based on studies limited by small sample size, retrospective design, or single-center experiences. To overcome the limited numbers of smaller single-center series, our study group Clinical, Multicenter Project of Analysis of Infective Endocarditis in Germany conducted this multicenter retrospective analysis to provide more reliable data on the clinical profile and postoperative course of patients undergoing cardiac surgery for NVE compared with PVE.

Our aim was to analyze the impact of NVE versus PVE on postoperative outcomes and long-term survival and to identify independent risk factors of 30-day, 1-year, and long-term mortality. A second objective was to investigate whether PVE alone or the clinical appearance at the time of the initial admission would be associated with an adverse long-term outcome.

PATIENTS AND METHODS

Study Population

This national multicenter retrospective analysis was conducted, including 4300 consecutive patients undergoing cardiac surgery for IE in 5 German cardiac surgery centers between 1994 and 2016 (Figure E1). There were no formal exclusion criteria. All consecutive patients undergoing cardiac surgery for IE were included. Acquired data included patients' demographics and comorbidities, manifestation of IE according to the recently modified Duke Criteria[16] (echocardiographic and microbiological data), perioperative data (cardiopulmonary bypass time [CPB], crossclamp time, and concomitant procedures), and relevant postoperative outcomes. IE-relevant complications were reported for the hospital stay. Long-term follow-up was obtained by review of hospital medical records and interview of the patient's physician with a completeness of 86.3% and a mean follow-up of 2.91 ± 3.8 years. The follow-up time for survival was measured from the date of operation to the date of death or the date of the last contact with the patient (date of discharge or date of last follow-up). The study protocol was approved by the institutional review boards. Individual informed consent was waived because of the retrospective nature of the collected data.

Operative Procedure

Cardiac surgery for IE was indicated according to the recent European Society of Cardiology guidelines for the management of IE[17] and conducted with the aim of achieving radical debridement of infected tissue. The type of surgery was performed according to the surgeon's preference and the extent of infection. Intraoperative transesophageal echocardiography was performed in all patients. Hemodynamic, catecholamine, and blood transfusion management was administered at the discretion of the attending cardiac surgeon and anesthesiologist.

Statistical Analysis

Unless otherwise indicated, continuous variables are described using mean values ± standard deviation or median (interquartile range) according to the normality of their distribution and compared using unpaired *t* test or Mann–Whitney *U* test as appropriate. Discrete variables are reported as percentages and tested by Pearson chi-square test or, when validity conditions were not satisfied, by Fisher exact test. Missing data were not imputed and assumed to be missing at random. Log-rank test was used to test for differences in long-term mortality between NVE and PVE. Resulting *P* values and additional Kaplan–Meier survival curves are presented. Potential risk factors for 30-day mortality (day 1-30) were assessed using logistic regression, potential risk factors for 1-year mortality (day 31-365), and long-term mortality (day >365) using Cox regression. For the Cox model, the proportional hazard assumption was tested and found valid by inspection of log-log-plots, scaled Schoenfeld residuals, and tests of the nonzero slope developed by Therneau and Grambsch.[18] We decided not to include the European System for Cardiac Operative Risk Evaluation (euroSCORE) in the univariable analysis because we expected a high collinearity between the separate variables included in the euroSCORE and the euroSCORE itself. After univariable analysis, all variables with a *P* value less than .05 were entered into the multivariable model using a forward selection (likelihood ratio, $p_{in} = .05$). Variable selection was based on score statistics in SPSS (IBM Corp, Armonk, NY). Results are presented as odds ratio for 30-day mortality or hazard ratio for 1-year and long-term mortality with corresponding 95% confidence interval and *P* value. All reported *P* values

are 2-sided. Statistical analyses were performed using SPSS Statistics Version 25 (IBM Corp).

Patients' Characteristics and Manifestation of Infective Endocarditis

The study population consisted of 3143 patients (73.1%) undergoing surgery for NVE and 1157 patients (26.9%) undergoing surgery for PVE. Patients with PVE presented with increased median age (69 [60-75] vs 63 [52-72] years; $P < .001$) and more comorbidities, such as hypertension (55% vs 46%; $P < .001$), diabetes (28% vs 25%; $P = .020$), hyperlipidemia (30% vs 18%; $P < .001$), pulmonary hypertension (20% vs 16%; $P < .001$), preoperative acute kidney injury (AKI) (Acute Kidney Injury Network stage ≥1) (41% vs 32%; $P < .001$), coronary artery disease (32% vs 23%; $P < .001$), and impaired left ventricular ejection fraction < 30% (5% vs 3%; $P < .001$). Contrarily, in patients with NVE preoperative stroke was more prevalent (22%) compared with patients with PVE (19%) ($P = .037$) and preoperative ventilation was more frequently noted in NVE (9%) than in PVE (6%) ($P = .002$) (Tables 1 and E1).

Echocardiographic and microbiological manifestation of IE are summarized in Tables 2 and E2. The aortic valve was most frequently involved in the entire cohort with a higher proportion of patients with PVE (75%) compared with NVE (59%). Inversely, patients with NVE were diagnosed more often with IE of the mitral valve (48% vs 32%; $P < .001$). The distribution of infected valves is depicted in Figure 1.

With regard to the microbiological findings, the 3 most detected microorganisms were Staphylococcus spp, Streptococcus spp, and Enterococcus spp. The proportion of Staphylococcus spp IE was comparable between NVE and PVE, with 23% in both groups ($P = .901$). Streptococcus spp was found more often in NVE (18% vs 7%; $P < .001$), whereas patients with PVE were more likely to have infections with Enterococcus spp (13% vs 9%; $P < .001$) (Table 2).

Concerning perioperative differences, CPB and crossclamp time were significantly longer in patients undergoing surgery for PVE compared with NVE (CPB time: 154 [114-217] vs 104 [77-142] minutes; $P < .001$;

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TABLE 1. Patients' demographics and preoperative characteristics

	All patients (n = 4300)	NVE (n = 3143)	PVE (n = 1157)	*P* value
Age, y	65 [54-73]	63 [52-72]	69 [60-75]	**<.001**
Sex				
Male	3100 (72%)	2274 (72%)	826 (71%)	.534
Female	1200 (28%)	869 (28%)	331 (29%)	.534
BSA	1.93 [1.79-2.07]	1.94 [1.79-2.08]	1.93 [1.80-2.06]	.241
Hypertension	2091 (49%)	1456 (46%)	635 (55%)	**<.001**
Diabetes	1113 (26%)	784 (25%)	329 (28%)	**.020**
Hyperlipidemia	924 (21%)	579 (18%)	345 (30%)	**<.001**
Smoking	829 (19%)	655 (21%)	174 (15%)	**<.001**
COPD	437 (10%)	308 (10%)	129 (11%)	.194
Peripheral artery disease	318 (7%)	221 (7%)	97 (8%)	.133
Pulmonary hypertension	724 (17%)	491 (16%)	233 (20%)	**<.001**
Preoperative AKI	1493 (35%)	1021 (32%)	472 (41%)	**<.001**
Hemodialysis	307 (7%)	223 (7%)	84 (7%)	.852
Preoperative stroke	898 (21%)	681 (22%)	217 (19%)	**.037**
Coronary artery disease	1076 (25%)	711 (23%)	365 (32%)	**<.001**
Myocardial infarction	212 (5%)	149 (5%)	63 (5%)	.344
LVEF				
≥50%	3122 (75%)	2334 (77%)	788 (70%)	**<.001**
≥30%-50%	883 (21%)	600 (20%)	283 (25%)	**<.001**
<30%	143 (3%)	85 (3%)	58 (5%)	**<.001**
NYHA				
I	411 (12%)	291 (11%)	120 (13%)	.271
II	1091 (32%)	796 (31%)	295 (33%)	.944
III	1348 (39%)	1002 (39%)	346 (38%)	.216
IV	588 (17%)	452 (18%)	136 (15%)	**.026**
euroSCORE	11 [6-20]	10 [5-18]	15 [9-32]	**<.001**
Preoperative ventilation	350 (8%)	281 (9%)	69 (6%)	**.002**

Data presented as median and interquartile range [IQR] or number (%), respectively. Bold indicates $P < .05$. *NVE*, Native valve endocarditis; *PVE*, prosthetic valve endocarditis; *BSA*, body surface area; *COPD*, chronic obstructive pulmonary disease; *AKI*, acute kidney injury; *LVEF*, left ventricular ejection fraction; *NYHA*, New York Heart Association; *euroSCORE*, European System for Cardiac Operative Risk Evaluation.

TABLE 2. Manifestation of infective endocarditis

	All patients (n = 4300)	NVE (n = 3143)	PVE (n = 1157)	*P* value
Echocardiography				
Left-sided IE				
Aortic valve	2727 (63)	1856 (59)	871 (75)	**<.001**
Mitral valve	1870 (43)	1495 (48)	375 (32)	**<.001**
Right-sided IE				
Tricuspid valve	263 (6)	233 (7)	30 (3)	**<.001**
Pulmonary valve	45 (1)	22 (1)	23 (2)	**<.001**
Double valve IE	609 (14)	439 (14)	170 (15)	.545
Triple valve IE	25 (1)	18 (1)	7 (1)	.901
Pacemaker-associated IE	49 (1)	34 (1)	15 (1)	.556
Presence of vegetation	2598 (60)	1949 (62)	649 (56)	**<.001**
Microbiology				
Positive blood culture	2682 (62)	1998 (64)	684 (59)	**.008**
Staphylococcus spp	998 (23)	731 (23)	267 (23)	.901
Streptococcus spp	656 (15)	572 (18)	84 (7)	**<.001**
Enterococcus spp	445 (10)	290 (9)	155 (13)	**<.001**
Focus	1733 (40)	1088 (35)	645 (56)	**<.001**
ENT	72 (2)	55 (2)	17 (1)	.525
Teeth	196 (5)	155 (5)	41 (4)	.053
Lungs	242 (6)	191 (6)	51 (4)	**.035**
Urological	244 (6)	180 (6)	64 (6)	.806
Intestine	241 (6)	200 (6)	41 (4)	**<.001**
Wound	193 (4)	146 (5)	47 (4)	.413
Septic embolism	1436 (33)	1061 (34)	375 (32)	.407
Brain	767 (18)	563 (18)	204 (18)	.831
Lungs	146 (3)	122 (4)	24 (2)	**<.004**
Spleen	810 (19)	566 (18)	244 (21)	**.022**
Kidney	339 (8)	240 (8)	99 (9)	.320

Data presented as number (%). Bold indicates $P < .05$. *NVE*, Native valve endocarditis; *PVE*, prosthetic valve endocarditis; *IE*, infective endocarditis; *ENT*, ear, nose, and throat.

crossclamp time: 104 [72-139] vs 70 [51-98] minutes; $P < .001$). In patients with PVE a concomitant ascending aortic or aortic root surgery was performed significantly more often compared with patients with NVE (37% vs 10%; $P < .001$), whereas patients with NVE underwent more concomitant coronary artery bypass grafting (13% vs 10%; $P = .021$) (Tables E3 and E4).

Clinical Outcomes

Postoperative clinical outcomes are depicted in Table 3. Cardiac surgery for PVE was associated with a significantly higher 30-day (19.6% vs 10.6%; $P < .001$) and 1-year mortality compared with NVE (36.4% vs 21.6%; $P < .001$). With regard to postoperative complications, the reexploration rate for bleeding did not differ after surgery for PVE and NVE (12% vs 11%; $P = .142$). The incidence of postoperative stroke (19% vs 16%; $P = .011$) and postoperative AKI requiring hemodialysis (20% vs 15%; $P < .001$) was higher after surgery for PVE compared with NVE. In addition, patients with PVE required a longer time of ventilation and had a higher tracheostomy rate (13% vs 9%; $P = .001$).

Kaplan–Meier survival analysis revealed a significantly decreased long-term survival of patients undergoing surgery for PVE compared with NVE (log-rank $P < .001$; Figure 2), even when patients with 30-day mortality were excluded (Figure E2). However, after Cox proportional hazards regression with multivariable adjustment, there was no significant difference in long-term survival between patients with PVE and patients with NVE (Figure 3).

Factors Associated With 30-Day, 1-Year, and Long-Term Mortality

Univariable analyses of preoperative and intraoperative risk factors for 30-day, 1-year, and long-term mortality are depicted in Tables E5 to E8. Multivariable analysis (MVA) revealed age more than 65 years, diabetes, chronic obstructive pulmonary disease, preoperative AKI, preoperative ventilation, and Staphylococcus spp IE as independent preoperative risk factors for 30-day mortality. Furthermore, the intraoperative variables CPB time more than 120 minutes and concomitant coronary artery bypass grafting were independently associated with 30-day mortality (Table 4). In addition, we performed MVA for patients undergoing surgery for NVE and PVE separately. Independent risk factors associated with 30-day mortality for patients undergoing surgery for NVE or PVE are depicted in Table E9.

MVA for 1-year mortality showed the same factors and the following independent preoperative risk factors: female sex, pulmonary hypertension, preoperative hemodialysis, preoperative stroke, coronary artery disease, any mitral valve IE, and presence of a vegetation. Infection with Staphylococcus spp was not independently predictive for 1-year mortality. Streptococcus spp was associated with lower 1-year mortality. Concerning intraoperative factors, CPB time more than 120 minutes and concomitant aortic surgery were independent risk factors for 1-year mortality. In both, MVAs for 30-day and 1-year mortality PVE itself were found to be independently predictive for 30-day and 1-year mortality, respectively (Table 4).

With regard to long-term mortality after the first year of operation, MVA revealed only preoperative and not intraoperative variables as risk factors

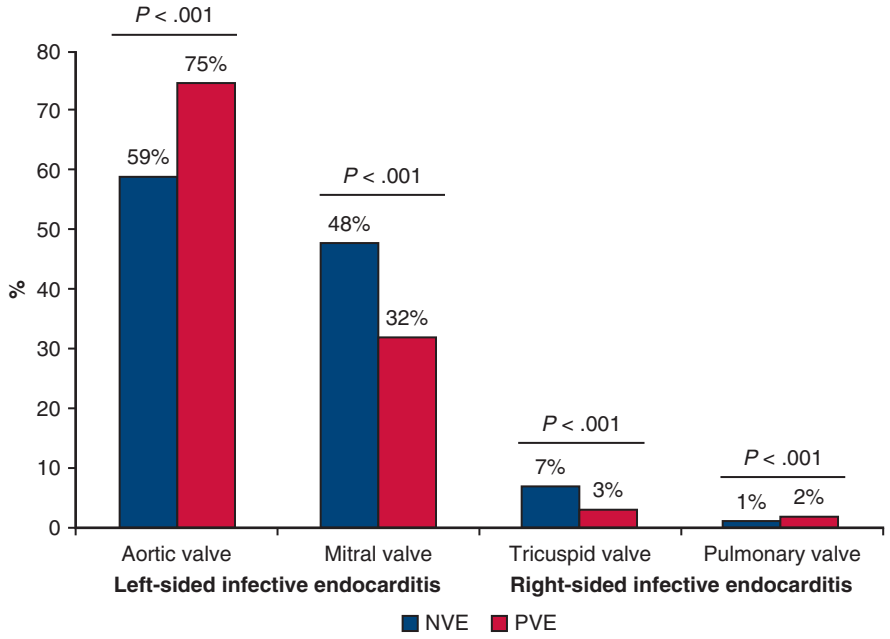


FIGURE 1. Distribution of affected valves in patients undergoing surgery for PVE compared with NVE. The aortic valve was most frequently affected in the entire cohort, with a higher proportion of patients undergoing surgery for PVE. Inversely, patients with NVE were more often diagnosed with IE of the mitral valve. *NVE*, Native valve endocarditis; *PVE*, prosthetic valve endocarditis.

for mortality. PVE was not independently predictive for long-term mortality (Table 4).

Subgroup Analysis of Aortic, Mitral, and Double Valve Infective Endocarditis

Kaplan–Meier analysis revealed significant differences of survival depending on the operated valve (log-rank + Bonferroni correction: $P = .015$) (Figure E3). We found a significantly decreased survival of patients with PVE of each entity (aortic, mitral, or double valve IE) compared with operations on the same valve with NVE (aortic NVE vs PVE log-rank: $P < .001$, mitral NVE vs PVE log-rank: $P < .001$, double valve NVE vs PVE log-rank: $P < .001$). Surgery for aortic NVE was associated with the best survival, whereas cardiac surgery for mitral NVE showed survival comparable to surgery for double valve NVE. Highest mortality rates were associated with mitral and double valve PVE.

Subgroup Analysis of Patients With Native Valve Endocarditis With First Versus Redo Surgery

With regard to patients with NVE with first operation compared with redo operation, 5.3% in the NVE group underwent redo surgery. The clinical characteristics and postoperative 30-day outcome of patients with NVE with first operation compared with redo operation are shown in Tables E10 and E11. The 30-day mortality is comparable in patients with first operation compared with redo operation (11.9% vs 13.3%, $P = .596$). In line with this, redo operation in patients with NVE could not be identified as a potential risk factor after univariable analysis and therefore did not enter MVA. We could identify advanced age more than 65 years, diabetes, chronic obstructive pulmonary disease, preoperative AKI, left ventricular ejection fraction less than 30%, preoperative ventilation, and Staphylococcal infection as independent risk factors for 30-day mortality in patients undergoing surgery for NVE (Table E9).

TABLE 3. Postoperative outcome of patients undergoing surgery for infective endocarditis

	All patients (n = 4300)	NVE (n = 3143)	PVE (n = 1157)	*P* value
30-d mortality	559 (13.0%)	332 (10.6%)	227 (19.6%)	**<.001**
1-y mortality	1099 (25.6%)	678 (21.6%)	421 (36.4%)	**<.001**
Reexploration	485 (11%)	341 (11%)	144 (12%)	.142
Postoperative stroke	708 (16%)	490 (16%)	218 (19%)	**.011**
Postoperative hemodialysis	695 (16%)	460 (15%)	235 (20%)	**<.001**
Tracheostomy	430 (10%)	285 (9%)	145 (13%)	**.001**
Time of ventilation (h)	17 [8-114]	14 [8-86]	26 [10-193]	**<.001**
ICU stay (d)	3 [1-5]	3 [1-5]	4 [2-7]	**<.001**
Hospital stay (d)	13 [8-21]	13 [8-19]	15 [9-24]	**<.001**

Data presented as median [IQR] or number (%), respectively. Bold indicates $P < .05$. *NVE*, Native valve endocarditis; *PVE*, prosthetic valve endocarditis; *ICU*, intensive care unit.

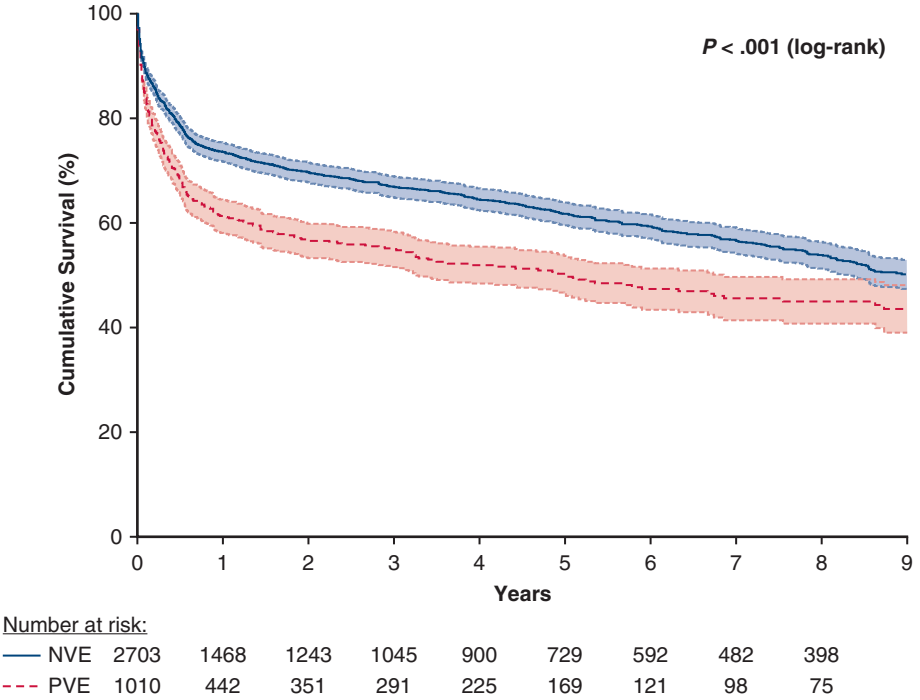


FIGURE 2. Kaplan–Meier survival curve depicting impaired long-term survival of patients undergoing surgery for PVE compared with NVE. Kaplan–Meier analysis shows a significantly lower survival of patients with PVE compared with NVE (log-rank $P < .001$). The impaired survival occurs especially within the first months after surgery. *NVE*, Native valve endocarditis; *PVE*, prosthetic valve endocarditis.

DISCUSSION

In this multicenter retrospective analysis, PVE accounted for 26.3% of all patients undergoing cardiac surgery for IE, reflecting a considerably higher proportion of PVE compared with earlier reports.[1,3] Consistent with the epidemiologic trends of IE in general,[19] the patient population with PVE has grown progressively older and presents with more severe preoperative conditions.[1]

Della Corte and colleagues[1] reported on stable 30-day mortality rates of approximately 20% for patients undergoing surgery for PVE over 3 eras. This is in line with the findings of Lalani and colleagues,[2] who hypothesized that several other factors reflecting changes in the epidemiology of PVE, such as higher patient age, cause of *S aureus*, and healthcare-associated infection, may contribute to the persistently high in-hospital and 1-year mortality rates.[2,20] Concordantly, we observed a decrease in mortality for patients undergoing surgery for NVE, whereas mortality rates for PVE stayed consistently high over years (Table E12). Thus, it seems that we still do not understand all aspects of PVE that lead to these considerably high mortality rates.

Previous research demonstrated a higher mortality rate of patients undergoing surgery for PVE (19%-50%) compared with NVE (7%-13%).[4-6] This is in line with our findings showing a significantly higher 30-day and 1-year mortality after surgery for PVE in comparison with NVE. Our observed 30-day mortality rate of 19.6% in the PVE group and 10.6% in the NVE group is comparable with results of these previous studies ($P < .001$). However, our data illustrate that 30-day mortality underestimates the risk of mortality significantly. Between 30 days and 1 year after the initial operation, an almost identical number of patients died, resulting in a 1-year mortality of 36.4% for PVE and 21.6% for patients with NVE ($P < .001$). Manne and associates[11] observed similar survival. They reported that although more than 90% survived up to 30 days after surgery, only 80% survived the first year, 82% of those with NVE and 77% of those with PVE. In line with this, others found a 1-year mortality rate of patients undergoing surgery for PVE between 27%[2] and 29%.[12]

Concerning long-term survival, our Kaplan–Meier analysis shows a significantly lower survival of patients with PVE compared with NVE (log-rank $P < .001$) (Figure 4, *A*). The Kaplan–Meier curve illustrates that the impaired survival occurs especially within the first months after surgery. Afterward, both survival curves run almost parallel. Likewise, Alonso-Valle and colleagues[12] observed the highest mortality rate during the first 3 months after hospital discharge. After this period, the survival of their patients remained stable.[12] This is also in line with previous work of Manne and colleagues[11] reporting on significantly higher in-hospital mortality for PVE compared with NVE, but similar long-term survival. However, after Cox proportional hazards regression with multivariable adjustment, there was

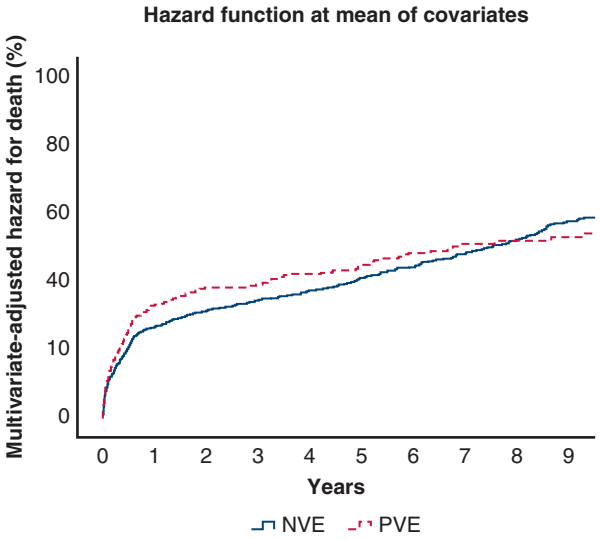


FIGURE 3. Comparable survival of patients undergoing surgery for PVE compared with NVE after Cox proportional hazards regression with multivariable adjustment for preoperative comorbidities. After Cox proportional hazards regression with multivariable adjustment, we found no significant difference in long-term survival between patients with PVE and NVE. *NVE*, Native valve endocarditis; *PVE*, prosthetic valve endocarditis.

no significant difference in long-term survival between PVE and NVE (Figure 4, *B*).

The higher observed early mortality rate might be attributed to the technically more demanding operations for PVE. Involvement of the aortic valve was high in both patients with NVE and patients with PVE, with a significantly higher proportion in the PVE group (75% vs 59%; $P < .001$). Previous reports showed that aortic PVE is frequently accompanied by perivalvular infection and aortic root destructions, which usually requires radical debridement and reconstruction.[9,21-23] As a surrogate marker for the higher complexity of surgery, CPB and crossclamp times were significantly longer in surgery for PVE than NVE. In addition, patients with PVE required a higher rate of concomitant aortic surgery (37% vs 10%; $P < .001$).

Besides intraoperative differences, several preoperative risk factors for adverse outcomes in patients undergoing surgery for IE have been identified.[1,13,14] Similar with our data, the study by Pericart and colleagues[13] revealed the following risk factors to be associated with mortality: increased age, mitral valve infection, Staphylococcus IE, vegetation, and stroke.

S aureus is the most frequently isolated microorganism in patients with IE in high-income countries and has been found in up to 30% of cases,[14,23,24] followed by coagulase-negative Staphylococci and Streptococci.[3,25] Infection with *S aureus* has been found to independently predict worse prognosis[10,26] because of its association with severe valvular damage, large vegetations, and

TABLE 4. Independent preoperative and intraoperative risk factors associated with 30-day, 1-year, and long-term mortality in patients undergoing surgery for infective endocarditis

Independent risk factors for 30-d mortality (Hosmer–Lemeshow test $P = .539$)		
	OR (95% CI)	***P* value**
Preoperative risk factors		
PVE	1.520 (1.150-2.009)	**.003**
Age >65 y	1.452 (1.111-1.898)	**.006**
Diabetes	1.635 (1.256-2.128)	**<.001**
COPD	1.557 (1.113-2.178)	**.010**
Preoperative AKI	1.777 (1.374-2.298)	**<.001**
LVEF <30%	2.581 (1.505-4.425)	**.001**
Preoperative ventilation	1.997 (1.419-2.810)	**<.001**
Staphylococcus spp IE	1.596 (1.236-2.059)	**<.001**
Intraoperative risk factors		
CPB time >120 min	1.395 (1.065-1.828)	**.016**
Concomitant CABG	1.405 (1.033-1.912)	**.030**
Independent risk factors for 1-y mortality (likelihood-ratio test $P < .001$)		
	HR (95% CI)	***P* value**
Preoperative risk factors		
PVE	1.262 (1.010-1.578)	**.040**
Age >65 y	1.643 (1.325-2.038)	**<.001**
Female sex	1.373 (1.117-1.688)	**.003**
Diabetes	1.523 (1.242-1.868)	**<.001**
COPD	1.497 (1.159-1.934)	**.002**
Pulmonary hypertension	1.339 (1.062-1.688)	**.014**
Preoperative AKI	1.564 (1.258-1.945)	**<.001**
Preoperative hemodialysis	1.743 (1.283-2.369)	**<.001**
Preoperative stroke	1.385 (1.127-1.703)	**.002**
Coronary artery disease	1.459 (1.189-1.791)	**<.001**
Preoperative ventilation	1.391 (1.050-1.843)	**.021**
Mitral valve IE	1.509 (1.225-1.859)	**<.001**
Vegetation	1.545 (1.078-2.214)	**.018**
Streptococcus spp IE	0.766 (0.587-1.000)	**.050**
Intraoperative risk factors		
CPB time >120 min	1.313 (1.051-1.640)	**.017**
Concomitant aortic surgery	1.598 (1.251-2.042)	**<.001**
Independent risk factors for long-term mortality (likelihood-ratio test $P < .001$)		
	HR (95% CI)	***P* value**
Preoperative risk factors		
Age >65 y	1.943 (1.534-2.460)	**<.001**
Diabetes	1.342 (1.040-1.732)	**.024**
Smoking	1.610 (1.256-2.065)	**<.001**
COPD	1.526 (1.111-2.096)	**.009**
Peripheral artery disease	1.920 (1.352-2.726)	**<.001**
Preoperative AKI	1.290 (1.006-1.654)	**.045**
Myocardial infarction	1.604 (1.086-2.370)	**.018**
LVEF <30%	1.857 (1.064-3.239)	**.029**
Preoperative ventilation	1.766 (1.188-2.625)	**.005**
Staphylococcus spp IE	1.335 (1.065-1.673)	**.012**

Bold indicates $P < .05$. *OR*, Odds ratio; *CI*, confidence interval; *PVE*, prosthetic valve endocarditis; *COPD*, chronic obstructive pulmonary disease; *AKI*, acute kidney injury; *LVEF*, left ventricular ejection fraction; *IE*, infective endocarditis; *CPB*, cardiopulmonary bypass; *CABG*, coronary artery bypass grafting; *HR*, hazard ratio.

ADULT

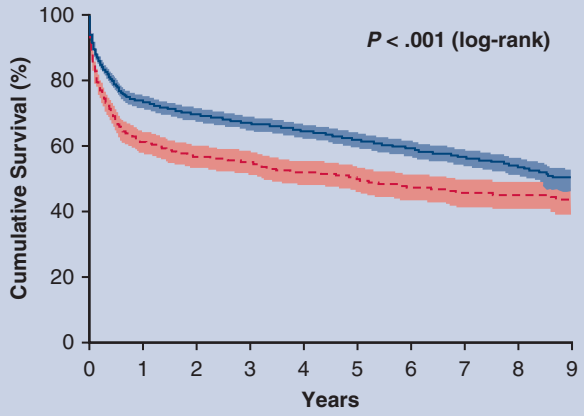
Methods

- Multicenter retrospective analysis
- 5 German cardiac surgery centers
- 1994-2016
- 4300 patients undergoing valve surgery for infective endocarditis (IE)

Results

Long-term survival

Impaired long-term survival of patients undergoing surgery for PVE

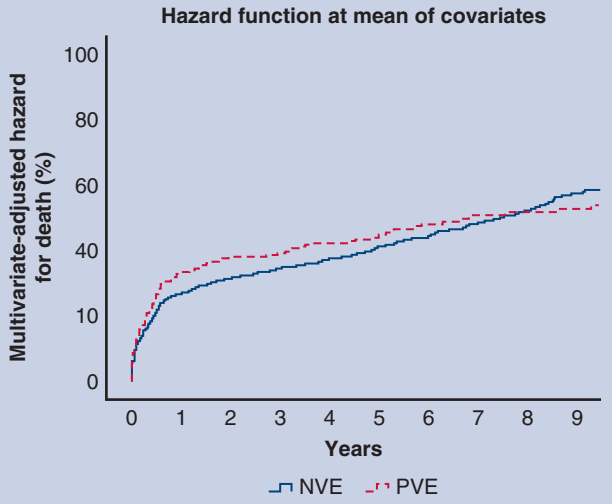


Number at risk:

NVE	2703	1468	1243	1045	900	729	592	482	398
PVE	1010	442	351	291	225	169	121	98	75

A

Comparable survival after Cox proportional hazards regression with multivariate adjustment



B

Implications

- Although PVE is associated with high mortality rates
  - 30-day mortality 19.6%
  - 1-year mortality 36.4%
- long-term survival is comparable with NVE

→ **Diagnosis of PVE alone, should not hinder surgeons from performing cardiac surgery**

FIGURE 4. A, Significantly decreased long-term survival of patients undergoing surgery for PVE compared with NVE ($P < .001$). B, After adjusting for preoperative comorbidities, long-term survival is comparable. *NVE*, Native valve endocarditis; *PVE*, prosthetic valve endocarditis.

embolic complications.[9,27,28] In line with this, our MVA revealed Staphylococcus spp IE as an independent risk factor for 30-day and long-term mortality. Pericart and colleagues[13] hypothesized that Staphylococcus may select a population with more comorbidities, such as nosocomial infection, hemodialysis, and chronic skin ulcers.

Endocarditis caused by Streptococcus spp is frequently related to community-acquired infections, including invasive orodental procedures, skin infections, and oral or gastrointestinal infections.[17,25] We found an association of Streptococcus spp IE with lower 1-year mortality, which is consistent with earlier reports of others.[1,13,14]

Nevertheless, despite improvements in diagnosis and treatment of PVE, morbidity, and mortality remain consistently high, underlining the necessity of further prospective studies regarding preventive and therapeutic strategies for this serious disease. One reason could be that Duke criteria have reduced sensitivity in patients with suspected

PVE.[23,29] In line with this, we observed that patients with PVE had a lower rate of positive blood cultures and less evidence of vegetations in echocardiography, which makes the diagnosis of PVE more difficult than of NVE. Therefore, we suggest that early detection and diagnosis of PVE are essential to prevent further perivalvular destruction. Thus, supplementary computed tomography imaging should be considered in suspected PVE with negative findings in echocardiography and blood cultures.

Study Limitations

Our study has several limitations that should be considered when interpreting the results. First, our cohort might be influenced by referral bias because most institutions are tertiary care centers. Thus, the results of the present study may not be generalizable. There might be potential bias based on center-specific experience and comfort level with increasingly complex procedures. Second, like in all multicenter studies, the heterogeneity in defining variables, in regional referral and practice patterns, and in data-collection methods might bias our results. Some variables had too many missing data and had to be removed from the analysis (eg, early vs late PVE, type of valve [mechanical/biologic], repair vs replacement, use of homografts, intravenous drug use, subgroups of Staphylococcus spp). Complete case analysis was performed, with the exception of operative data (CPB and crossclamp time) and the isolated microorganisms, which were not consistently recorded by all centers. Third, our loss to follow-up rate was 13.7%. Fourth, because of missingness in the variables included in the final multivariable Cox model, the sample of patients included in the final model is lower than in the original population. However, because the amount of missing data is similar between groups, it seems unlikely that missing data will bias our results too much. Fifth, despite the use of Cox proportional hazards regression with multivariable adjustment, other variables not evaluated may confound the results of this analysis. Variables without statistical or causal association but importance from the surgical point of view (eg, septic embolism or right- vs left-sided IE) were not forced into the MVA. Nevertheless, we report on a large number of patients undergoing surgery for PVE compared with NVE, and we hope our data may contribute to a better knowledge of the clinical course and outcome of these complex patients.

CONCLUSIONS

We provide evidence that although PVE remains associated with a high 30-day and 1-year mortality, PVE alone is not independently associated with adverse long-term outcome. Therefore, we recommend that the diagnosis of PVE alone should not hinder surgeons from performing surgery in this complex patient population. We recommend patients with suspected PVE should be transferred to tertiary high-volume centers with experienced cardiac surgeons and a multidisciplinary team with the relevant expertise in diagnostics and treatment of PVE.

Webcast

You can watch a Webcast of this AATS meeting presentation by going to: https://aats.blob.core.windows.net/media/19%20AM/Monday_May6/205BD/205BD/S77%20-%20Endocarditis/285-205BD-May6-1515-1530-Weber.mp4.

Conflict of Interest Statement

Dr Borger has received speaker honoraria and served as a consultant for Edwards Lifesciences, Medtronic, and Abbott. Dr Akhyari has received a St Jude Medical Research grant and has reported relationships to Edwards Lifesciences and Medtronic. All other authors have nothing to disclose with regard to commercial support.

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Key Words: native valve endocarditis, NVE, prosthetic valve endocarditis, PVE

Discussion

Dr Sary F. Aranki *(Boston, Mass)*. This is a multicenter retrospective analysis of a large cohort of 4300 surgical patients with IE. The authors' objective was to compare outcomes of native versus PVE, and they believe that having a large number from a multicenter group may give them better answers than a small number of patients from a single center as they stated in their introduction. Follow-up was 86% complete, and survival was measured from the date of surgery to the date of death or the date of last contact with the patient. How accurate is this method? Is there a national German registry for death from which you can get more accurate data?

Dr Carolyn Weber *(Cologne, Germany)*. We don't have a registry just for endocarditis, but there is a German registry for death. But it's usually difficult to get the death just for endocarditis, so we have our follow-up in each cardiac center.

Dr Aranki. My second question concerns the timing of surgery. What was the guiding principle between the time of diagnosis and the time of surgery? Was there a difference in timing among the 5 participating centers and has the timing of surgery changed over the last 22 years of the study?

Dr Weber. Normally, there are 3 main indications for surgery, which is heart failure, uncontrolled infection, or a lot of vegetation. Surgery in all of the centers was performed according to the European guidelines for surgery. I think, especially in PVE, there is a higher rate of paravalvular infection, so this is usually uncontrolled infection, and therefore those with PVE undergo operation earlier than those with native valve infection.

Dr Aranki. The incidence of silent embolism was 33%. The majority were in the brain and spleen. There is no more evidence that silent emboli incidence is probably as high as symptomatic emboli. Do you do any positron emission tomography imaging studies to determine if there is silent emboli and will that affect the timing of surgery?

Dr Weber. We don't do a computed tomography scan of the brain routinely in patients with endocarditis. What we do is just computed tomography scans in patients with a suspected endocarditis with a negative echo. So this is often in patients with PVE. But I think silent embolism would not make any change in our treatment.

Dr Aranki. You have no information on the incidence of annular abscesses or type of surgery performed: aortic root replacement, homografts, or type of prosthesis. Can you explain?

Dr Weber. This is one of the limitations in a multicenter analysis, because some of the variables were not assessed in every center. In Cologne in the PVE group, it's 60% of paravalvular infection and in NVE it is approximately 30%, so a higher rate of paravalvular infection patients with PVE. Therefore, concomitant aortic surgery was higher in patients with PVE.

Dr Aranki. Do you have any data on intravenous drug use, what we call the opioid crisis? This is a hot topic in IE that has a major impact on the development of multiple PVE with worse outcomes. Also, there is a small but an increasing number of immunosuppressed patients with fungal endocarditis. Do you have any information about these patients?

Dr Weber. We don't have the same problem with intravenous drug abuse in Europe like you have in the United

States. So it's still at just approximately 10% with right-sided IE, and of them, about one-third with intravenous drug abuse. So we don't have the same number of intravenous drug abuse-related endocarditis. And your other question about fungal endocarditis, this is a small number of patients (∼2% or 3%).

Dr Aranki. Do you think you have achieved your goal of having more number of patients gives you a more accurate diagnosis even though you don't have much complete information?

Dr Weber. I think it's not always better to have more patients, but we could just see the same results in smaller studies. I think the most important thing is timely diagnosis of patients with PVE, because they often present atypically, and if they have negative findings that could show all in echo. So we suggest, and this is the only thing that we can say that we would do because of our study, especially in patients with PVE, you should consider early computed tomography to see if these patients have a periannular infection, which you can't detect on echocardiography.

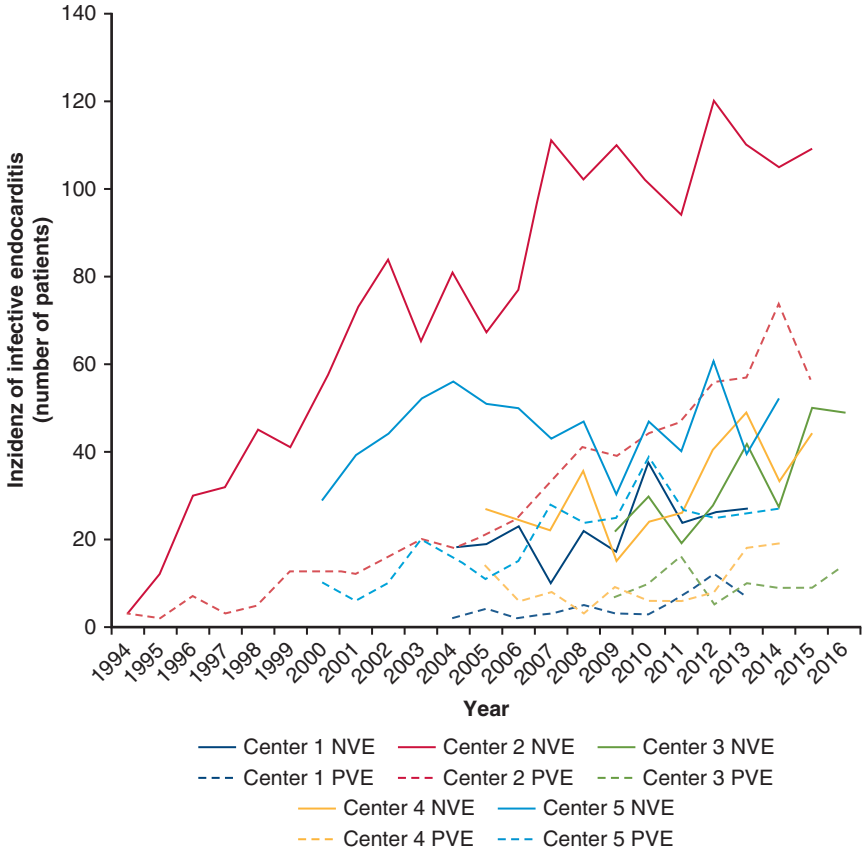


FIGURE E1. Incidence of NVE and PVE per year for each center. We observed an increase in the incidence of IE in all centers, with an increase in NVE and PVE. *NVE*, Native valve endocarditis; *PVE*, prosthetic valve endocarditis.

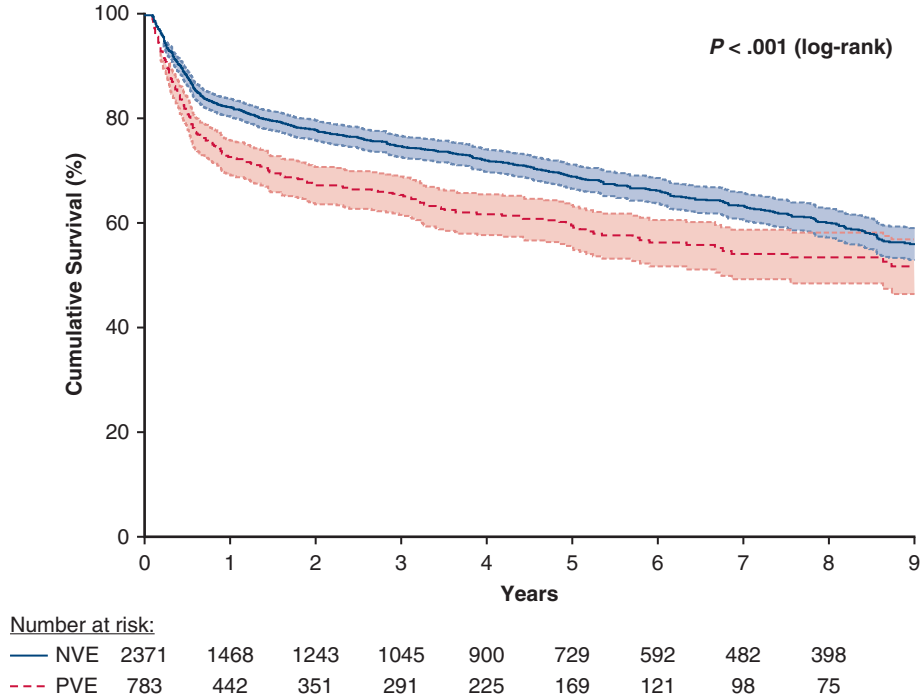
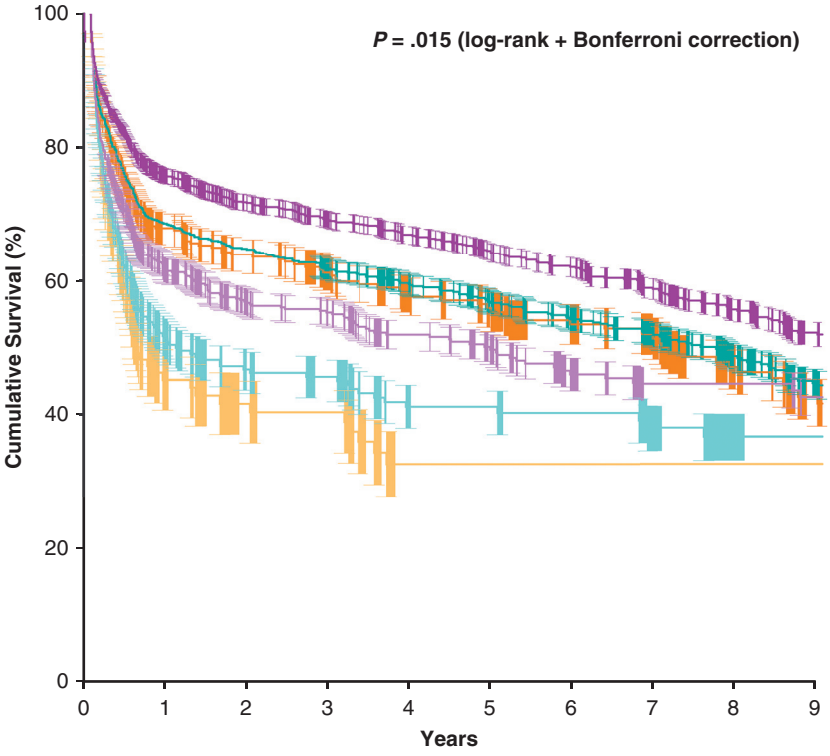


FIGURE E2. Kaplan–Meier analysis for patients undergoing surgery for PVE compared with NVE excluding patients with 30-day mortality. Even in patients surviving the first 30 days postoperatively, there remains a significantly decreased long-term survival of patients with PVE compared with NVE (log rank $P < .001$). *NVE*, Native valve endocarditis; *PVE*, prosthetic valve endocarditis.



Number at risk:

Aortic NVE	1595	939	796	675	577	468	381	309	251
Aortic PVE	757	327	255	212	161	123	85	70	55
Mitral NVE	1320	625	522	425	370	297	252	210	210
Mitral PVE	332	115	91	79	59	45	38	35	29
Double NVE	413	213	179	142	120	94	88	77	61
Double PVE	152	41	32	29	18	15	13	12	10

FIGURE E3. Subgroup analysis of patients with NVE and PVE in aortic, mitral, and double valve IE. Kaplan–Meier analysis revealed significant differences of survival depending on the operated valve (log-rank + Bonferroni correction: $P = .015$). We found a significantly decreased survival of patients with PVE of each entity (aortic, mitral, or double valve IE) compared with operations on the same valve with NVE (aortic NVE vs PVE log-rank: $P < .001$, mitral NVE vs PVE log-rank: $P < .001$, double valve NVE vs PVE log-rank: $P < .001$). *NVE*, Native valve endocarditis; *PVE*, prosthetic valve endocarditis.

TABLE E1. Patients' demographics and preoperative characteristics including missing values

	All patients (n = 4300)		NVE (n = 3143)		PVE (n = 1157)		*P* value
Age, y	65 [54-73]	(1)	63 [52-72]	(1)	69 [60-75]	(0)	**<.001**
Sex							
Male	3100 (72%)	(0)	2274 (72%)	(0)	826 (71%)	(0)	.534
Female	1200 (28%)	(0)	869 (28%)	(0)	331 (29%)	(0)	.534
BSA	1.93 [1.79-2.07]	(114)	1.94 [1.79-2.08]	(92)	1.93 [1.80-2.06]	(22)	.241
Hypertension	2091 (49%)	(0)	1456 (46%)	(0)	635 (55%)	(0)	**<.001**
Diabetes	1113 (26%)	(0)	784 (25%)	(0)	329 (28%)	(0)	**.020**
Hyperlipidemia	924 (21%)	(0)	579 (18%)	(0)	345 (30%)	(0)	**<.001**
Smoking	829 (19%)	(0)	655 (21%)	(0)	174 (15%)	(0)	**<.001**
COPD	437 (10%)	(0)	308 (10%)	(0)	129 (11%)	(0)	.194
Peripheral artery disease	318 (7%)	(0)	221 (7%)	(0)	97 (8%)	(0)	.133
Pulmonary hypertension	724 (17%)	(0)	491 (16%)	(0)	233 (20%)	(0)	**<.001**
Preoperative AKI	1493 (35%)	(0)	1021 (32%)	(0)	472 (41%)	(0)	**<.001**
Hemodialysis	307 (7%)	(0)	223 (7%)	(0)	84 (7%)	(0)	.852
Preoperative stroke	898 (21%)	(0)	681 (22%)	(0)	217 (19%)	(0)	**.037**
Coronary artery disease	1076 (25%)	(0)	711 (23%)	(0)	365 (32%)	(0)	**<.001**
Myocardial infarction	212 (5%)	(0)	149 (5%)	(0)	63 (5%)	(0)	.344
LVEF		(152)		(124)		(28)	
≥50%	3122 (75%)		2334 (77%)		788 (70%)		**<.001**
≥30%-50%	883 (21%)		600 (20%)		283 (25%)		**<.001**
<30%	143 (3%)		85 (3%)		58 (5%)		**<.001**
NYHA		(859)		(601)		(258)	
I	411 (12%)		291 (11%)		120 (13%)		.271
II	1091 (32%)		796 (31%)		295 (33%)		.944
III	1348 (39%)		1002 (39%)		346 (38%)		.216
IV	588 (17%)		452 (18%)		136 (15%)		**.026**
euroSCORE	11 [6-20]	(605)	10 [5-18]	(461)	15 [9-32]	(144)	**<.001**
Preoperative ventilation	350 (8%)	(0)	281 (9%)	(0)	69 (6%)	(0)	**.002**

Data presented as median [IQR] or number (%), respectively. Bold indicates $P < .05$. *NVE*, Native valve endocarditis; *PVE*, prosthetic valve endocarditis; *BSA*, body surface area; *COPD*, chronic obstructive pulmonary disease; *AKI*, acute kidney injury; *LVEF*, left ventricular ejection fraction; *NYHA*, New York Heart Association; *euroSCORE*, European System for Cardiac Operative Risk Evaluation.

TABLE E2. Manifestation of infective endocarditis including missing values

	All patients (n = 4300)		NVE (n = 3143)		PVE (n = 1157)		*P* value
Echocardiography							
Left-sided IE							
Aortic valve	2727 (63%)	(0)	1856 (59%)	(0)	871 (75%)	(0)	**<.001**
Mitral valve	1870 (43%)	(0)	1495 (48%)	(0)	375 (32%)	(0)	**<.001**
Right-sided IE							
Tricuspid valve	263 (6%)	(0)	233 (7%)	(0)	30 (3%)	(0)	**<.001**
Pulmonary valve	45 (1%)	(0)	22 (1%)	(0)	23 (2%)	(0)	**<.001**
Double valve IE	609 (14%)	(0)	439 (14%)	(0)	170 (15%)	(0)	.545
Triple valve IE	25 (1%)	(0)	18 (1%)	(0)	7 (1%)	(0)	.901
Pacemaker-associated IE	49 (1%)	(0)	34 (1%)	(0)	15 (1%)	(0)	.556
Presence of vegetation	2598 (60%)	(0)	1949 (62%)	(0)	649 (56%)	(0)	**<.001**
Microbiology							
Positive blood culture	2682 (62%)	(0)	1998 (64%)	(0)	684 (59%)	(0)	**.008**
Isolated microorganism		(1866)		(1336)		(530)	
Staphylococcus spp	998 (23%)		731 (23%)		267 (23%)		.901
Streptococcus spp	656 (15%)		572 (18%)		84 (7%)		**<.001**
Enterococcus spp	445 (10%)		290 (9%)		155 (13%)		**<.001**
Focus	1733 (40%)	(0)	1088 (35%)	(0)	645 (56%)	(0)	**<.001**
ENT	72 (2%)	(0)	55 (2%)	(0)	17 (1%)	(0)	.525
Teeth	196 (5%)	(0)	155 (5%)	(0)	41 (4%)	(0)	.053
Lungs	242 (6%)	(0)	191 (6%)	(0)	51 (4%)	(0)	**.035**
Urological	244 (6%)	(0)	180 (6%)	(0)	64 (6%)	(0)	.806
Intestine	241 (6%)	(0)	200 (6%)	(0)	41 (4%)	(0)	**<.001**
Wound	193 (4%)	(0)	146 (5%)	(0)	47 (4%)	(0)	.413
Septic embolism	1436 (33%)	(0)	1061 (34%)	(0)	375 (32%)	(0)	.407
Brain	767 (18%)	(0)	563 (18%)	(0)	204 (18%)	(0)	.831
Lungs	146 (3%)	(0)	122 (4%)	(0)	24 (2%)	(0)	**<.004**
Spleen	810 (19%)	(0)	566 (18%)	(0)	244 (21%)	(0)	**.022**
Kidney	339 (8%)	(0)	240 (8%)	(0)	99 (9%)	(0)	.320

Data presented as number (%). Bold indicates $P < .05$. *NVE*, Native valve endocarditis; *PVE*, prosthetic valve endocarditis; *IE*, infective endocarditis; *ENT*, ear, nose, and throat.

TABLE E3. Operative data

	All patients (n = 4300)	NVE (n = 3143)	PVE (n = 1157)	*P* value
CPB time (min)	115 [83-161]	104 [77-142]	154 [114-217]	**<.001**
Crossclamp time (min)	78 [55-198]	70 [51-98]	104 [72-139]	**<.001**
Concomitant surgery				
Aorta	736 (17%)	305 (10%)	431 (37%)	**<.001**
CABG	528 (12%)	408 (13%)	120 (10%)	**.021**

Data presented as median [IQR] or number (%), respectively. Bold indicates $P < .05$. *NVE*, Native valve endocarditis; *PVE*, prosthetic valve endocarditis; *CPB*, cardiopulmonary bypass; *CABG*, coronary artery bypass grafting.

TABLE E4. Operative data including missing values

	All patients (n = 4300)		NVE (n = 3143)		PVE (n = 1157)		*P* value
CPB time (min)	115 [83-161]	(1006)	104 [77-142]	(695)	154 [114-217]	(311)	**<.001**
Crossclamp time (min)	78 [55-198]	(1036)	70 [51-98]	(707)	104 [72-139]	(329)	**<.001**
Concomitant surgery							
Aorta	736 (17%)	(0)	305 (10%)	(0)	431 (37%)	(0)	**<.001**
CABG	528 (12%)	(0)	408 (13%)	(0)	120 (10%)	(0)	**.021**

Data presented as median [IQR] or number (%), respectively. Bold indicates $P < .05$. *NVE*, Native valve endocarditis; *PVE*, prosthetic valve endocarditis; *CPB*, cardiopulmonary bypass; *CABG*, coronary artery bypass grafting.

TABLE E5. Univariable analysis of pre- and intraoperative risk factors associated with 30-day mortality in patients undergoing surgery for infective endocarditis

	OR (95% CI)	*P* value
Preoperative risk factors		
PVE	1.563 (1.392-1.754)	**<.001**
Age >65 y	1.380 (1.286-1.482)	**<.001**
Female sex	1.158 (1.015-1.322)	**.033**
Hypertension	1.005 (0.926-1.092)	.897
Diabetes	1.653 (1.467-1.863)	**<.001**
Hyperlipidemia	1.163 (1.002-1.350)	.051
Smoking	0.667 (0.542-0.820)	**<.001**
COPD	1.368 (1.090-1.718)	.008
Peripheral artery disease	1.436 (1.104-1.868)	.007
Pulmonary hypertension	1.347 (1.136-1.597)	.001
Preoperative AKI	1.668 (1.522-1.827)	**<.001**
Hemodialysis	2.416 (1.896-3.080)	**<.001**
Preoperative stroke	1.102 (0.943-1.288)	.228
Coronary artery disease	1.480 (1.306-1.678)	**<.001**
Myocardial infarction	2.010 (1.472-2.745)	**<.001**
LVEF ≥50%	0.822 (0.770-0.878)	**<.001**
LVEF ≥30%-50%	1.477 (1.271-1.717)	**<.001**
LVEF <30%	2.721 (1.893-3.909)	**<.001**
Preoperative ventilation	2.083 (1.669-2.600)	**<.001**
Aortic valve IE	1.005 (0.939-1.076)	.881
Mitral valve IE	1.099 (1.000-1.208)	.057
Tricuspid valve IE	0.828 (0.571-1.201)	.317
Pulmonary valve IE	0.576 (0.207-1.603)	.284
Pacemaker-associated IE	1.710 (0.879-3.325)	.111
Presence of vegetation	0.914 (0.853-0.979)	**.006**
Staphylococcus spp IE	1.406 (1.255-1.576)	**<.001**
Streptococcus spp IE	0.660 (0.518-0.840)	**<.001**
Enterococcus spp IE	0.803 (0.608-1.061)	.115
Septic embolism	0.951 (0.844-1.072)	.407
Intraoperative risk factors		
CPB time >120 min	1.416 (1.304-1.538)	**<.001**
Crossclamp time >90 min	1.383 (1.246-1.535)	**<.001**
Concomitant aortic surgery	1.391 (1.179-1.641)	**<.001**
Concomitant CABG	1.349 (1.104-1.649)	**.004**

Bold indicates $P < .05$. *OR*, Odds ratio; *CI*, confidence interval; *PVE*, prosthetic valve endocarditis; *COPD*, chronic obstructive pulmonary disease; *AKI*, acute kidney injury; *LVEF*, left ventricular ejection fraction; *IE*, infective endocarditis; *CPB*, cardiopulmonary bypass; *CABG*, coronary artery bypass grafting.

TABLE E6. Univariable analysis of preoperative and intraoperative risk factors associated with 1-year mortality in patients undergoing surgery for infective endocarditis

	HR (95% CI)	*P* value
Preoperative risk factors		
PVE	1.510 (1.328-1.716)	**<.001**
Age >65 y	1.511 (1.403-1.626)	**<.001**
Female sex	1.364 (1.201-1.548)	**<.001**
Hypertension	1.385 (1.298-1.477)	**<.001**
Diabetes	1.925 (1.698-2.181)	**<.001**
Hyperlipidemia	1.486 (1.293-1.707)	**<.001**
Smoking	0.969 (0.817-1.149)	.715
COPD	1.875 (1.507-2.332)	**<.001**
Peripheral artery disease	2.373 (1.859-3.028)	**<.001**
Pulmonary hypertension	1.527 (1.286-1.814)	**<.001**
Preoperative AKI	1.704 (1.539-1.886)	**<.001**
Hemodialysis	3.415 (2.616-4.459)	**<.001**
Preoperative stroke	1.699 (1.485-1.943)	**<.001**
Coronary artery disease	1.697 (1.494-1.929)	**<.001**
Myocardial infarction	1.564 (1.081-2.263)	**.018**
LVEF ≥50%	0.903 (0.854-0.955)	**<.001**
LVEF ≥30%-50%	1.304 (1.102-1.541)	**.002**
LVEF <30%	1.900 (1.208-2.989)	**.005**
Preoperative ventilation	2.318 (1.815-2.960)	**<.001**
Aortic valve IE	1.002 (0.935-1.073)	.955
Mitral valve IE	1.222 (1.116-1.339)	**<.001**
Tricuspid valve IE	0.983 (0.695-1.389)	.922
Pulmonary valve IE	0.252 (0.061-1.041)	.390
Pacemaker-associated IE	1.311 (0.604-2.844)	.493
Presence of vegetation	1.273 (1.216-1.333)	**<.001**
Staphylococcus spp IE	1.296 (1.153-1.457)	**<.001**
Streptococcus spp IE	0.530 (0.424-0.664)	**<.001**
Enterococcus spp IE	1.165 (0.947-1.433)	**.152**
Septic embolism	1.399 (1.269-1.543)	**<.001**
Intraoperative risk factors		
CPB time >120 min	1.402 (1.287-1.526)	**<.001**
Crossclamp time >90 min	1.410 (1.272-1.562)	**<.001**
Concomitant aortic surgery	1.669 (1.416-1.967)	**<.001**
Concomitant CABG	1.825 (1.507-2.211)	**<.001**

Bold indicates $P < .05$. *HR*, Hazard ratio; *CI*, confidence interval; *PVE*, prosthetic valve endocarditis; *COPD*, chronic obstructive pulmonary disease; *AKI*, acute kidney injury; *LVEF*, left ventricular ejection fraction; *IE*, infective endocarditis; *CPB*, cardiopulmonary bypass; *CABG*, coronary artery bypass grafting.

TABLE E7. Univariable analysis of pre- and intraoperative risk factors associated with long-term in patients undergoing surgery for infective endocarditis

	HR (95% CI)	*P* value
Preoperative risk factors		
PVE	0.957 (0.908-1.010)	.127
Age >65 y	1.123 (1.068-1.181)	**<.001**
Female sex	1.049 (0.990-1.112)	.089
Hypertension	1.093 (1.043-1.146)	**<.001**
Diabetes	1.122 (1.048-1.201)	**<.001**
Hyperlipidemia	1.080 (1.017-1.146)	.007
Smoking	1.137 (1.068-1.210)	**<.001**
COPD	1.347 (1.188-1.528)	**<.001**
Peripheral artery disease	1.387 (1.193-1.612)	**<.001**
Pulmonary hypertension	1.171 (1.082-1.268)	**<.001**
Preoperative AKI	1.073 (1.012-1.138)	.013
Hemodialysis	1.138 (0.959-1.349))	.078
Preoperative stroke	1.081 (1.016-1.151)	**.009**
Coronary artery disease	1.156 (1.081-1.237)	**<.001**
Myocardial infarction	1.387 (1.153-1.669)	**<.001**
LVEF ≥50%	0.923 (0.864-0.987)	**.011**
LVEF ≥30%-50%	1.053 (0.984-1.126)	.114
LVEF <30%	1.294 (1.015-1.650)	**.005**
Preoperative ventilation	1.155 (1.018-1.312)	**.008**
Aortic valve IE	0.972 (0.923-1.023)	.263
Mitral valve IE	1.054 (1.003-1.109)	**.035**
Tricuspid valve IE	1.046 (0.947-1.156)	.341
Pulmonary valve IE	0.810 (0.745-0.881)	**.029**
Pacemaker-associated IE	0.944 (0.781-1.140)	.594
Presence of vegetation	1.134 (1.083-1.188)	**<.001**
Staphylococcus spp IE	1.079 (1.011-1.153)	**.019**
Streptococcus spp IE	0.946 (0.888-1.007)	.091
Enterococcus spp IE	1.021 (0.943-1.105)	.604
Septic embolism	1.014 (0.965-1.065)	.585
Intraoperative risk factors		
CPB time >120 min	0.970 (0.922-1.020)	.236
Crossclamp time >90 min	0.973 (0.923-1.026)	.318
Concomitant aortic surgery	0.935 (0.882-0.991)	**.038**
Concomitant CABG	1.114 (1.023-1.214)	**.005**

Bold indicates $P < .05$. *HR*, Hazard ratio; *CI*, confidence interval; *PVE*, prosthetic valve endocarditis; *COPD*, chronic obstructive pulmonary disease; *AKI*, acute kidney injury; *LVEF*, left ventricular ejection fraction; *IE*, infective endocarditis; *CPB*, cardiopulmonary bypass; *CABG*, coronary artery bypass grafting.

TABLE E8. Nonsignificant independent risk factors for mortality

	Score	*P* value
30-d mortality		
Female sex	2.236	.135
Smoking	3.584	.058
Peripheral artery disease	0.136	.712
Pulmonary hypertension	1.190	.275
Hemodialysis	0.827	.363
Coronary artery disease	0.110	.740
Myocardial infarction	2.855	.091
LVEF ≥50%	2.416	.120
LVEF ≥30%-50%	2.416	.120
Presence of vegetation	2.576	.108
Streptococcus spp IE	1.536	.215
Crossclamp time >90 min	0.001	.975
Concomitant aortic surgery	0.214	.644
1-y mortality		
Hypertension	1.674	.196
Hyperlipidemia	0.382	.536
Peripheral artery disease	3.177	.075
Myocardial infarction	0.065	.799
LVEF ≥50%	2.870	.090
LVEF ≥30%-50%	2.218	.136
LVEF <30%	0.488	.485
Staphylococcus spp IE	0.177	.674
Septic embolism	0.309	.578
Crossclamp time >90%	0.043	.835
Concomitant CABG	0.197	.657
Long-term mortality		
Hypertension	0.152	.696
Hyperlipidemia	0.039	.843
Pulmonary hypertension	2.205	.138
Preoperative stroke	2.580	.108
Coronary artery disease	1.367	.242
Mitral valve IE	3.741	.053
Pulmonary valve IE	2.338	.126
Presence of vegetation	0.478	.489
Streptococcus spp IE	0.004	.950
Concomitant aortic surgery	1.157	.282
Concomitant CABG	0.003	.958

LVEF, Left ventricular ejection fraction; *IE*, infective endocarditis; *CABG*, coronary artery bypass grafting.

TABLE E9. Independent preoperative and intraoperative risk factors associated with 30-day mortality in patients with native valve endocarditis and prosthetic valve endocarditis

	NVE		PVE		
	OR (95% CI)	*P* value		OR (95% CI)	*P* value
Preoperative risk factors			Preoperative risk factors		
Age >65 y	1.475 (1.067-2.040)	**.019**	Age >65 y	1.683 (1.040-2.724)	**.034**
Diabetes	1.880 (1.358-2.603)	**<.001**	Preoperative AKI	1.954 (1.270-3.005)	**.002**
COPD	1.570 (1.030-2.393)	**.036**	Myocardial infarction	2.468 (1.046-5.825)	**.039**
Preoperative AKI	1.680 (1.212-2.328)	**.002**	Preoperative ventilation	2.872 (1.506-5.479)	**.001**
LVEF <30%	3.439 (1.664-7.105)	**.001**			
Preoperative ventilation	1.860 (1.238-2.795)	**.003**			
Staphylococcus spp IE	1.735 (1.262-2.386)	**.001**			
Intraoperative risk factors			Intraoperative risk factors		
Concomitant CABG	1.564 (1.084-2.257)	**.017**	Crossclamp time >90 min	2.828 (1.687-4.741)	**<.001**

Bold indicates $P < .05$. *NVE*, Native valve endocarditis; *PVE*, prosthetic valve endocarditis; *OR*, odds ratio; *CI*, confidence interval; *COPD*, chronic obstructive pulmonary disease; *AKI*, acute kidney injury; *LVEF*, left ventricular ejection fraction; *LVEF*, left ventricular ejection fraction; *CABG*, coronary artery bypass grafting*IE*, infective endocarditis.

TABLE E10. Characteristics of patients with native valve endocarditis with first compared with redo operation

	NVE with first operation (n = 2965)	NVE with redo operation (n = 178)	*P* value
Age, y	63 [52-72]	66 [55-75]	**<.009**
Sex			
Male	2139 (72%)	135 (76%)	.284
Female	862 (28%)	43 (24%)	.284
BSA	1.93 [1.79-2.08]	1.97 [1.84-2.11]	**.026**
Hypertension	1359 (46%)	97 (55%)	**<.024**
Diabetes	722 (24%)	62 (35%)	**.002**
Hyperlipidemia	514 (17%)	65 (37%)	**<.001**
Smoking	621 (21%)	34 (20%)	.556
COPD	290 (10%)	18 (10%)	.885
Peripheral artery disease	195 (7%)	26 (15%)	**<.001**
Pulmonary hypertension	455 (15%)	36 (20%)	.082
Preoperative AKI	943 (32%)	78 (44%)	**.001**
Hemodialysis	208 (7%)	15 (8%)	.476
Preoperative stroke	649 (22%)	32 (18%)	.219
Coronary artery disease	637 (22%)	74 (42%)	**<.001**
Myocardial infarction	128 (4%)	21 (12%)	**<.001**
LVEF			
≥50%	2223 (78%)	111 (65%)	**<.001**
≥30%-50%	553 (19%)	47 (27%)	**.012**
<30%	71 (3%)	14 (8%)	**<.001**
NYHA			
I	274 (11%)	17 (12%)	.889
II	759 (32%)	37 (27%)	.151
III	937 (39%)	65 (46%)	.171
IV	431 (18%)	21 (15%)	.312
euroSCORE	9 [5-17]	17 [10-35]	**<.001**
Preoperative ventilation	270 (9%)	11 (6%)	.184

Bold indicates $P < .05$. *NVE*, Native valve endocarditis; *BSA*, body surface area; *COPD*, chronic obstructive pulmonary disease; *AKI*, acute kidney injury; *LVEF*, left ventricular ejection fraction; *NYHA*, New York Heart Association; *euroSCORE*, European System for Cardiac Operative Risk Evaluation.

TABLE E11. Postoperative 30-day outcome patients with native valve endocarditis with first compared with redo operation

	NVE with first operation (n = 2965)	NVE with redo operation (n = 178)	*P* value
30-d mortality	310 (12%)	22 (13%)	.596
Reexploration	314 (11%)	27 (15%)	.056
Postoperative stroke	458 (15%)	32 (18%)	.366
Postoperative hemodialysis	418 (14.1)	42 (24%)	**<.001**
Tracheostomy	261 (9%)	24 (14%)	**.035**
Time of ventilation (h)	14 [7-79]	38 [10-187]	**<.001**
ICU stay (d)	2 [1-5]	5 [2-10]	**<.001**
Hospital stay (d)	13 [8-19]	15 [8-25]	**.017**

Bold indicates $P < .05$. *NVE*, Native valve endocarditis; *ICU*, intensive care unit.

ADULT

TABLE E12. Annual 30-day mortality rate of patients undergoing surgery for prosthetic valve endocarditis compared with native valve endocarditis

	1994	1995	1996	1997	1998	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016
NVE	0%	8%	20%	19%	7%	15%	12%	16%	11%	16%	18%	12%	9%	15%	12%	13%	9%	14%	11%	12%	11%	7%	6%
PVE	0%	0%	0%	0%	40%	15%	31%	25%	26%	12%	26%	20%	23%	24%	19%	15%	18%	21%	26%	21%	22%	18%	35%

NVE, Native valve endocarditis; *PVE*, prosthetic valve endocarditis.