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Surgical treatment of prosthetic valve endocarditis: a 7-year single-center experience

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ABSTRACT

Introduction: Prosthetic valve endocarditis remains a serious life threatening condition, affecting 1-6% of patients with valve prosthesis and requiring repeated valve replacement.

Methods: A retrospective study included cases histories of 33 patients undergoing valve replacement surgery for PVE at a single-center between 2010 and 2017.

Results: The mean age at presentation was 67.27 ± 14.07 years, without gender dependance. More than half of patients (54.5%) had late endocarditis. 12 (34.3%) patients had mechanical prosthesis infection, 23 (65.7%) - bioprosthesis infection. Aortic prosthesis was the most frequently infected one (72.7%). 12.1% of cases had double prosthetic valve endocarditis. In-hospital mortality rate was 21.2%. Postoperative complications occurred in 23 (69.7%) patients, with shock and other complications being the most frequent ones. Only EuroScore was significantly associated with in-hospital mortality (21.67 ± 3.06 vs 13.47 ± 4.01, p=0.003). Multivariable logistic regression analysis showed that perioperative shock after reoperation (OR=44.824, p=0.025) and longer cardiopulmonary bypass time (OR=0.989; p=0.022) was independently associated with in-hospital mortality.

Conclusions: PVE surgical treatment has a high risk of in-hospital mortality and clinical outcomes, so information about preoperative parameters associated with mortality and the frequency of early outcomes may have additional value in understanding PVE.

Keywords: endocarditis, prosthetic valve, prosthetic valve endocarditis, surgical treatment

INTRODUCTION

Despite diagnostic and treatment advances prosthetic valve endocarditis (PVE) still remains a serious life threatening condition [1]. PVE affects 1 - 6% of patients with valve prosthesis and constitutes 16 – 34% of all cases of infective endocarditis [2–4]. The best strategy for PVE treatment is still discussed; some patients may recuperate with medical treatment, but many of them need repeated valve replacement [5]. Surgical treatment for PVE is recommended for heart failure or cardiogenic shock, severe prosthetic valve dysfunction or paravalvular complications, persistent bacteremia with resistant pathogens and persistent vegetations 10 mm or larger after an embolic event, according to 2015 American Heart Association and European Society of Cardiology guidelines for the diagnosis and management of infective endocarditis [6, 7].

METHODS

A retrospective study included case histories of 33 patients scheduled for PVE surgical treatment between 2010 - 2017 in Lithuanian University of Health Sciences Kaunas Clinics in Kaunas, Lithuania. All patients underwent reoperative valve replacement. Data from case histories was collected: clinical characteristics, comorbidities, before and after surgery echocardiographic data, surgery data, prosthetic types, microbial agents, early in-hospital postoperative complications and mortality. Based on European Society of Cardiology guidelines [7] , PVE was classified as early, when occurring within a 1 year from primary valvular surgery and late, with onset after 1 year. An additional category of perioperative PVE was added, when occured recently after primary surgery within in-hospital period or rehabilitation. Statistical analysis was performed with MS Excel 2010 and IBM SPSS 22.0. Basic characteristics of categorical variables presented in percentage (%). Descriptive statistical data results were described as mean ± standard deviation (SD) for normally distributed parameters, median and 25th - 75th percentile (interquartile range (IQR) for asymmetrically distributed data. Comparisons were made using Stjudent t-test, Chi square tests and Mann-Whitney test for nonparametric data. P value < 0.05 was considered statistically significant. Univariate analyses were performed to to assess differences among groups of survivors and non-survivors. Multivariable logistic regression analysis was used to identify independent risk factors for in-hospital mortality. All variables significantly associated in univariate analysis ($p < 0.05$) and variables that were clinically relevant with $p < 0.1$ were introduced in multivariable model.

RESULTS

Basic characteristics

During the study period 33 patients received surgical PVE treatment, which resulted in reoperation and resternotomy. The mean age of patients during reoperation was 67.27 ± 14.07 years (range 20 - 87 y), the median age was 70.0 (interquartile range 61.5 - 77.0), with no statistically significant difference between gender ($p = 0.149$). Male / female ratio was 17 / 16 (51.5 / 48.5%).

Preoperative characteristics

The preoperative clinical characteristics and information about first valve replacement surgery is shown in Table 1. Data about previously implanted prosthetic valve types was not available for all patients. Data of pathogenic microorganism was also available only for 24 cases out of 33, because of the lack of access to microbiological examination results. For most patients - 31 (93.9%) - this was a first redo operation, while 2 (6.1%) patients had a second PVE induced redo procedure (re-reoperation). Of those, for one patient first redo surgery was performed before study time interval (before 2010), statistical calculations included the second PVE re-reoperation. Another patient had both PVE episodes between 2010-2017, however, only first PVE - first redo surgery - was included in the statistical calculations. The most frequent comorbidities was as follows: hypertension (75.8%), ischaemic heart disease (66.7%), atrial fibrillation (39.4%) and dyslipidaemia (33.3%). Most patients had III NYHA class heart failure (36.4%). Almost one third (30.3%) of patients

experienced previous valve repair procedures before valve replacement surgery.

Comorbidities, n (%)	
Hypertension	25 (75.8)
Diabetes	8 (24.2)
Obesity	9 (27.3)
Renal insufficiency	4 (12.1)
Anaemia	6 (18.2)
Gout	4 (12.1)
Rheumatic heart disease	7 (21.1)
Ischaemic heart disease	22 (66.7)
Heart failure (NYHA class), n (%)	
I-II / III-IV	10/21 (30.3/63.7)
No heart failure	2 (6.0)
Previous pacemaker implantation, n (%)	6 (18.2)
Atrial fibrillation, n (%)	13 (39.4)
Previous embolic stroke, n (%)	5 (15.2)
Pulmonary oedema, n (%)	2 (6.1)
Shock at presentation, n (%)	2 (6.1)
Embolic stroke at presentation, n (%)	2 (6.1)
Previous procedures, n (%)	
Previous valve repair	10 (30.3)
Previous CABG	9 (27.3)
Previous PTCA	8 (24.2)
Previous CABG+PTCA	1 (3.0)
More than one previous cardiac surgery	4 (12.1)
Pre-operative echocardiographic data, n (%)	

Valve replacement data, n (%)	
Number of valves replaced	
1	29 (87.9)
2	4 (12.1)
Type of replaced valve	
Aortic	24 (72.7)
Mitral	5 (15.2)
Aortic+mitral	4 (12.1)
Type of prosthesis infected *	
Biological	23 (65.7)
Mechanical	12 (34.3)
Type of bioprosthesis **	
Biocor	6 (27.3)
St.Jude	11 (50.0)
Medtronic	3 (13.6)
Other (Hancock II, Toronto SPV)	2 (9.1)
Type of mechanical prosthesis ***	
St.Jude	4 (80)
Other (Sorin Bicarbon)	1 (20)
CABG associated with valve replacement	6 (18.2)
Microbial agent, n (%) ****	
Streptococcus spp.	2 (8.3)
Staphylococcus spp.	7 (29.2)
Enterococcus spp.	3 (12.5)
Other	2 (8.3)

Ejection fraction (%)	47.06 ± 9.62		Negative	10 (41.7)
Abscess	19 (57.6)		PVE classification according to time from primary valvular surgery, n (%)	
Vegetation	20 (60.6)		Early PVE	10 (30.3)
Peri-prosthetic leak	12 (36.4)		Late PVE	18 (54.5)
Abnormal space around prosthesis	7 (21.2)		Perioperative PVE	5 (15.2)
Pulmonary hypertension	6 (18.2)			

Table 1. Preoperative clinical characteristics of PVE patients.
* Prosthetic type data includes one or more prosthesis replaced in the same patient with not all data available. ** Data on type of bioprosthesis is available in 22 cases out of 23. *** Data on type of mechanical prosthesis is available only in 5 cases out of 12.
**** Microbial agent data available only for 24 cases. CABG - coronary artery bypass grafting. PTCA - percutaneous transluminal coronary angioplasty. PVE - prosthetic valve endocarditis.

More than half of the patients (54.5%) had late PVE (> 1 year since primary surgery), almost one third (30.3%) early PVE and 15.2% perioperative PVE. Most patients had single prosthetic valve infection (87.9%), with prosthetic aortic valve being the most frequently infected one in 72.7% cases. Only 12.1% cases had double prosthetic valve endocarditis with 2 replaced valves (aortic and mitral). Biological prostheses were infected more often (65.7%), comparing with mechanical ones (34.3%). St. Jude was the most common bioprosthesis - half of the cases (50.0%), the same type being the most common mechanical prosthesis as well (4 cases out of 5). Considering microbial data, 41.7% of cases was regarded as negative for pathogenic microorganisms. *Staphylococcus spp.* was present in 29.2%, *Enterococcus spp.* in 12.5% and *Streptococcus spp.* in 8.3% of cases.

Surgery data

In 29 (87.9%) patients, a single valve was re-replaced, in 4 (12.1%) patients - 2 valves. In summary, 37 prosthesis used for 33 patients. PVE surgery data is shown in Table 2.

Surgery type, n (%)	
Elective	7 (21.2)
Urgent	23 (69.7)
Emergency	3 (9.1)
Single valve PVE, n (%)	29 (87.9)
Double valve PVE, n (%)	4 (12.1)
Infected valve type, n (%)	
Mitral	5 (15.2)
Aortic	24 (72.7)

Mitral+aortic	4 (12.1)
Cardiopulmonary bypass time (min) *	174.26±94.94 (130.0 [107.0-246.0])
Aortic cross-clamp time (min)*	99.87±51.87 (80.0 [61.0-132.0])
Type of aortic prosthesis reimplanted, n (%), n=28	
Biological/ mechanical	25/3 (89.3/10.7)
Type of mitral prosthesis reimplanted, n (%), n=9	
Biological/ mechanical	7/2 (77.822.2)
Type of bioprosthesis, n (%), n=31	
Biocor	10 (32.3)
St.Jude	6 (19.4)
Medtronic	13 (41.9)
Other	2 (6.5)
Type of mechanical prosthesis, n (%), n=5	
St.Jude	1 (20.0)
Other	4 (80.0)
Main associated procedures, n (%)	
Ascending aorta or root replacement	8 (24.2)
CABG	4 (12.1)
CABG+ascending aorta or root replacement	2 (6.1)
EuroSCORE	14.59±4.79 (14.0 [10.0-18.25])
Post-operative echocardiography, n=27	
Ejection fraction (%)	45.15±10.43 (50.0 [40.0-51.25])
Good function of prosthesis	26 (96.3)
Peri-prosthetic leak	1 (3.7)

Table 2. Surgery data of PVE patients. * Cardiopulmonary bypass time and aortic cross-clamp time was available in 31 cases. CABG - coronary artery bypass grafting.

Early outcomes

Early in-hospital mortality was 21.2% (7 patients). Causes of death determined as follows: acute cardiovascular insufficiency - 4 (57.1%) patients, sepsis - 1 (14.3%), multi-organ failure - 1 (14.3%), cardiogenic shock - 1 (14.3%) patient. Postoperative complications (including death as complication) occurred in 23 (69.7%) patients. The most frequent complication was classified as other (such as atrial fibrillation, pneumonia, pneumothorax, pericarditis, anaemia, a.radialis pseudoaneurysm, pulmonary embolisation) - 7 (21.2%). Other complications include: shock - 6 (18.2%), re-opening for bleeding - 3 (9.1%), pacemaker implantation demand - 3 (9.1%), mediastinitis - 2 (6.1%), neurological complications - 1 (3.0%), acute respiratory failure - 1 (3.0%), sepsis - 1 (3.0%), suppuration of the sternum - 1 (3.0%).

Risk factor analysis

A comparison of two groups (in-hospital non-survivors and survivors) at univariate analysis is demonstrated in Table 3. In univariable analysis only EuroScore showed a significant association with mortality (21.67 ± 3.06 vs 13.47 ± 4.01, p=0.003). There was no statistically significant difference in mortality among different types of prosthesis implanted, difference aetiology of microorganisms, other comorbidities or other variables (p>0.05).

Variable	Number (%) of patients		p value	OR (95% CI)
	Non-survivors (n=7 (21.1%)	Survivors (n=26 (78.8%)		
Female gender	5 (71.4)	11 (42.3)	0.171	0.293 (0.048-1.801)
Age	71.86±5.55	66.04±15.45	0.126	
Hypertension	7 (100)	18 (69.2)	0.092	0.720 (0.564-0.919)
Diabetes	3 (42.9)	5 (19.2)	0.32*	3.15 (0.528-18.803)
Obesity	3 (42.9)	6 (23.10)	0.358*	2.5 (0.433-14.430)
Renal insufficiency	1 (14.1)	3 (11.5)	0.843*	1.278 (0.112-14.587)
Anaemia	2 (28.6)	4 (15.4)	0.584*	2.2 (0.311-15.548)
Gout	2 (28.6)	2 (7.7)	0.190*	4.8 (0.540-42.632)
Rheumatic heart disease	2 (28.6)	5 (19.2)	0.623*	1.68 (0.249-11.322)
Ischaemic heart disease	6 (85.7)	16 (61.5)	0.228	3.75 (0.391-35.923)

Previous pacemaker implantation	2 (28.6)	4 (15.4)	0.584*	2.2 (0.311-15.548)
Atrial fibrillation	2 (28.6)	11 (42.3)	0.676*	0.545 (0.089-3.350)
Previous embolic stroke	0 (0)	5 (19.2)	0.559*	1.333 (1.077-1.651)
Pulmonary edema	0 (0)	2 (7.7)	0.449*	1.292 (1.068-1.562)
Shock at presentation	1 (14.3)	1 (3.8)	0.384*	4.167 (0.227-76.601)
Embolic stroke at presentation	0 (0)	2 (7.7)	0.449*	1.292 (1.068-1.562)
Previous valve repair	2 (28.6)	8 (30.8)	0.911*	0.9 (0.143-5.662)
Previous CABG	3 (42.9)	6 (23.1)	0.358*	2.5 (0.433-14.430)
Previous PTCA	2 (28.6)	6 (23.1)	0.763*	1.333 (0.204-8.708)
Previous CABG+PTCA	0 (0)	1 (3.8)	0.788*	1.28 (1.066-1.538)
Previous more than 1 cardiac surgery	1 (14.3)	3 (11.5)	0.843*	1.278 (0.112-14.587)
Ejection fraction	41.43±7.48	48.58±9.69	0.081	
Abscess	4 (57.1)	15 (57.7)	0.979*	0.978 (0.181-5.283)
Vegetation	5 (71.4)	15 (57.7)	0.509	1.833 (0.299-11.259)
Peri-prosthetic leak	2 (28.6)	10 (38.5)	0.629*	0.64 (0.104-3.951)
Abnormal space around prosthesis	2 (28.6)	5 (19.2)	0.623*	1.68 (0.249-11.322)
Pulmonary hypertension	2 (28.6)	4 (16.0)	0.590*	2.1 (0.297-14.873)
CABG associated with primary valve surgery	3 (42.9)	3 (11.5)	0.093*	0.174 (0.025-1.187)
PVE classification according to time				
Early PVE	3 (42.9)	7 (26.9)	0.646*	2.036 (0.361-11.479)

Late PVE	3 (42.9)	15 (57.7)	0.674*	0.550 (0.102--2.972)
Perioperative PVE	1 (14.3)	4 (15.4)	0.876*	0.917 (0.086-9.805)
Type of infected valve				
Aortic	4 (57.1)	20 (76.9)	0.358*	0.4 (0.069-2.309)
Mitral	2 (28.6)	3 (11.5)	0.282*	3.067 (0.401-23.440)
Aortic+mitral	1 (14.3)	3 (11.5)	0.843*	1.278 (0.112-14.589)
Type of infected prosthesis				
Bioprosthetic valve	5 (83.3)	17 (65.4)	0.393	2.647 (0.267-26.245)
Mechanical valve	1 (16.7)	9 (34.6)	0.637*	0.378 (0.038-3.746)
Type of bioprosthesis infected				
Biocor	0 (0)	6 (24.0)	0.296*	1.368 (1.084-1.728)
St.Jude	3 (42.9)	7 (28.0)	0.648	1.929 (0.341-10.910)
Medtronic	0 (0)	3 (12.0)	0.336*	1.318 (1.074-1.619)
Other (Hancock II, Toronto SPV)	1 (14.3)	1 (4.0)	0.395*	4.0 (0.217-73.618)
Type of mechanical prosthesis infected				
St.Jude	0 (0)	3 (11.5)	0.346*	1.304 (1.071-1.589)
Other (Sorin Bicarbon)	0 (0)	1 (3.8)	0.598*	1.280 (1.066-1.538)
Type of bioprosthesis reimplanted				
Biocor	1 (16.7)	8 (30.8)	0.648*	0.450 (0.045-4.501)
St.Jude	2 (28.6)	2 (7.7)	0.190*	4.80 (0.540-42.632)
Medtronic	3 (42.9)	10 (38.5)	0.833*	1.20 (0.221-6.521)

Other	1 (14.3)	1 (3.8)	0.387*	4.167 (0.227-76.601)
Type of mechanical prosthesis reimplanted				
St.Jude	0 (0)	1 (3.8)	0.598*	1.280 (1.066-1.538)
Other	0 (0)	2 (7.7)	0.449*	1.292 (1.068-1.562)
CABG associated with prosthesis replacement,	3 (42.9)	3 (11.5)	0.093*	0.174 (0.025-1.187)
Microbial agent, n (%) *****				
Streptococcus spp.	1 (20.0)	1 (5.0)	0.367*	4.75 (0.243-92.97)
Staphylococcus spp.	1 (20.0)	6 (30.0)	0.656*	0.583 (0.053-6.372)
Enterococcus spp.	0 (0)	3 (15.0)	0.356*	1.294 (1.032-1.623)
Other	1 (20.0)	1 (5.0)	0.367*	4.75 (0.243-92.97)
Negative	1 (20.0)	9 (45.0)	0.615*	0.306 (0.029-3.242)
Surgery type, n (%)				
Elective	1 (14.3)	6 (23.1)	0.614*	0.556 (0.55-5.570)
Urgent	4 (57.1)	18 (69.20)	0.661*	0.593 (0.107-3.286)
Emergency	1 (14.3)	2 (7.7)	0.523*	2.0 (0.154-25.917)
Cardiopulmonary bypass time (min) *	252.57±131.292	149.28±69.06	0.085	
Aortic cross-clamp time (min)*	122.71±67.17	93.21±46.12	0.190	
EuroSCORE	21.67±3.06	13.47±4.01	**0.003**	
Perioperative complications				
Shock	3 (42.9)	3 (11.5)	0.093*	5.750 (0.843-39.241)

Table 3. Univariable analysis of factor associated with in-hospital mortality. * means p-value originated from Fisher's exact test, all other p-values originated from χ^2 test. OR - odds ratio. CI - confidence interval.

Multivariable logistic regression analysis demonstrated that mortality was independently associated with perioperative complication - shock, whereas shorter cardiopulmonary bypass time was associated with survival (Table 4). The model had an area under the ROC curve of 0.742.

Variables	B	P-value	OR (95% CI)
Shock*	3.803	0.025	44.824 (1.619-1241.285)
Cardiopulmonary bypass time	-0.019	0.013	0.981 (0.966-0.996)

Table 4. Multivariable logistic regression analysis of factors associated with in-hospital mortality in PVE patients. OR - odds ratio, CI - confidence interval, PVE - prosthetic valve endocarditis.* Perioperative shock after reoperation.

DISCUSSION

Meta-analysis of 32 studies demonstrated that PVE surgical treatment is associated with lower risk of mortality comparing with medical treatment [8], but re-reoperation due to PVE still is of relatively high morbidity and mortality risk.

Our results confirmed high in-hospital mortality rates with 21.2%. Larger cohort studies found similar rates, with 19.2% reported by Della Corte et al [9], 21.5% by Luciani et al [10] and slightly lower percentage of 11.9% by Kim et al [11]. The present study was similar to Hee-Hwa et al [12], where Chinese registry included 34 surgically treated PVE patients over a 7-year period with 28% overall hospital mortality and 61% morbidity.

Regarding pathogenic microorganisms responsible for PVE, our study demonstrated that *Staphylococcus spp.* was present only up to 29.2% cases. This result is lower than previously reported results with *Staphylococcus spp.* present in more than half of cases [10]. This may be due to 41.7% of negative for pathogenic microorganism in the present study. However, our study confirmed that *Staphyloccoccus spp*. lacks association with mortality or other clinical outcomes, as demonstrated in other studies [9, 11].

The most frequently infected single valve was aortic (72.7%), which complies with other authors well [9-11]. However, in-hospital mortality is not affected by the type of valve implanted.Only one factor demonstrated to be associated with hospital mortality by univariate analysis (EuroScore). The strongest predictors of mortality in multivariable logistic regression analysis were perioperative shock after reoperation and longer cardiopulmonary bypass time, the latter complies with Kim et al [11] well and may be only as an indicator of more complicated and time-consuming surgery in high-risk procedure of PVE patients. Association of perioperative shock after reoperation with mortality implies that haemodynamic condition is one of the possible determinants of worse early outcome for PVE surgery [9]. However, preoperative renal failure [9], female sex, multivalvular intervention, periprosthetic abscess, urgent indication [10] and severe heart failure [12] were not confirmed to predict mortality in the present study, as in other studies, probably due to small number of in-hospital deaths and small sample size, the same reasons as other small number studies comply with [12].

However, study has some limitations. First of all, small sample size of 33 patients from a single center, comparing with other PVE surgical treatment involving studies with large cohorts and multicenter analysis [9, 10]. This may be due to chosen study period of 7 years between 2010 - 2017. Second limitation was due to data availability restrictions, such as limited accessibility to microbial examination results or

lack of information about type of reimplanted prosthesis. Missing data had to be removed from the analysis. Third, due to short period of only 7 years, comparison of different time periods as in [9] was not possible, but would have provided additional information about time-related trends in presentation and outcomes [9].

In conclusion, PVE has a high risk of in-hospital mortality and clinical outcomes, so information about preoperative parameters associated with mortality and the frequency of early outcomes may have additional value in understanding PVE.

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