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JOURNAL OF Cardiovascular Medicine and Cardiology OPEN ACCESS JOURNAL

ISSN: 2455-2976 DOI: https://dx.doi.org/10.17352/jcmc

Research Article

Clinical features and outcome of prosthetic pulmonary valve infective endocarditis

Daniel Pastor[1#], Juan Carlos Castillo[2*], Rafael González[2], José López-Aguilera[2], Dolores Mesa[2], Manuel Anguita[2] and Manuel Pan[2]

[1]Cardiology Department, Hospital Universitario Reina Sofía. Avda. Menéndez Pidal s/n. 14004 Córdoba. Spain

[2]Maimonides Biomedical Research Institute of Cordoba, Spain

[#]Contributed to the Article Equally

Received: 19 September, 2022
Accepted: 24 September, 2022
Published: 26 September, 2022

***Corresponding author:** Juan Carlos Castillo, MD, Cardiology Department. Hospital Universitario Reina Sofía. Avda. Menéndez Pidal s/n. 14004 Córdoba. Spain, E-mail: juanc.castillo.dominguez@juntadeandalucia.es

ORCID: https://orcid.org/0000-0002-3164-0823

Keywords: Endocarditis; Pulmonary valve; Prostheses

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Abstract

Background: Infective endocarditis is a serious complication in patients with prostheses in the right ventricle outflow tract. The aim of our study is to assess clinical features in these patients.

Methods: We have analyzed all cases of prosthetic pulmonary valve infective endocarditis (PPVIE) and compared them to the rest of the patients with IE. Since the year 2000, 375 cases of IE have been diagnosed in our center and nine patients had a PPVIE.: 3 patients with Melody percutaneous prostheses, 5 with a homograft (3 after a Rastelli procedure, 2 a Ross procedure), and 1 patient with a heterograft (Contegra conduit).

Results: Mean age of PPVIE patients was 31±15 years old and 89% were male. A presumed portal of entry could only be identified in 4 of the 9 patients with PPVIE. The most common was a dental origin (3 patients). A causative microorganism was detected in all but one PPVIE patient: 3 *S.viridans*, 2 *S.aureus*, 2 coagulase-negative *staphylococci,* and 1 *enterococcus*. Most patients suffered complications during the in-hospital phase: 7 out of 9 PPVIE patients (78 vs.75% of the rest of IE patients), the most common congestive heart failure (5 patients), and persistent sepsis (4 patients). Six patients were operated on during hospitalization (67 vs. 55%) with a mean time from admission to surgery of 15 days. In-hospital mortality was similar (22 vs. 26%).

Conclusions: Prevalence of PPVIE is low, with a clinical outcome, surgery rate, and survival similar to the rest of patients with IE.

Introduction

Pulmonary valve prostheses are used for the treatment of congenital heart diseases and long-term complications of previous surgical procedures. Percutaneous pulmonary valve implantation has become an alternative to open-heart surgery in congenital heart disease. Many young patients with congenital aortic valvar stenosis undergo the Ross procedure. In both situations, right ventricular outflow tract dysfunction frequently occurs because of the limited lifespan of the biological material. Therefore, pulmonary valve prostheses either surgical or percutaneous are required.

Although a rare complication, infection of pulmonary prostheses may occur. However, there is a paucity of data regarding such a situation. Right-sided infective endocarditis (IE) accounts for only 5–13.8% of all cases of IE, affecting the pulmonary valve in only 2.4% [1-3].

Our aim is to analyze the clinical characteristics and outcomes of patients with prosthetic pulmonary valve infective endocarditis (PPVIE). A second objective was to investigate differences in the clinical presentation, microbiological findings, and prognosis of such patients compared to other forms of IE.

Citation: Pastor D, Castillo JC, González R, López-Aguilera J, Mesa D, et al. (2022) Clinical features and outcome of prosthetic pulmonary valve infective endocarditis. J Cardiovasc Med Cardiol 9(3): 024-027. DOI: https://dx.doi.org/10.17352/2455-2976.000183

Methods

Between January 2000 and December 2021, 375 cases of IE in non-intravenous drug users were consecutively diagnosed and treated in our center. Our hospital is a tertiary center that during the study period was the referral center for cardiovascular surgery in the Spanish provinces of Córdoba and Jaén (the area includes 3 regional hospitals in Córdoba and 4 hospitals in Jaén). Patients diagnosed with IE in our institution are traditionally admitted to the cardiology service only. Patients enrolled in this study came from the emergency room, internal medicine, or echocardiography service. Thirty-four patients (9%) were referred from other hospitals. The incidence of patients from other centers remained constant during the study period. Initially, the diagnosis of IE was made according to the modified Duke criteria [5]. Since 2004, we have applied the European Cardiology Society's diagnostic criteria [6]. A total of 9 patients were admitted to our center with IE following interventional or surgical pulmonary valve replacement. Infected conduits were stented bovine yugular vein grafts (Melody valve; Medtronic, Minneapolis, MN, USA) in 3 patients, a Contegra Conduit in 1 patient, and homografts (3 patients with a Rastelli procedure and 2 for a previous Ross procedure) in 5 patients.

Specific antibiotic treatment was maintained during the active phase for at least 4 weeks in native valve IE patients and 6 weeks for prosthetic valve IE. Antibiotics were administered intravenously at the hospital except for 23 patients that followed a program of home-setting parenteral treatment. Indications for surgery during the active phase (early surgery) were the appearance of severe heart failure due to a valve or prosthesis dysfunction; persistent sepsis despite correct antibiotic treatment; the appearance of local complications such as abscesses, pseudoanaeurysms, and fistulas; repeated embolisms; and cases caused by aggressive organisms that generally did not respond to antibiotics, such as fungi, Coxiella spp, and Brucella spp. Indications for surgery did not differ over the study period. We defined urgent surgery as that which could not be postponed>24h without putting the patient's life at risk, and elective surgery as that which could be delayed a few days without increasing the risk to the patient's life. All patients who survived the active phase of IE were included in database follow up and for those of which we had no information, telephone contact was established to avoid missing data.

The study protocol was approved by the institutional review board. Individual informed consent was waived due to the retrospective nature of the collected data.

Continuous variables are expressed as mean ± standard deviation and compared using Student's t-test for unpaired data. Categorical variables are presented as numbers (percentage) and compared using the $\chi 2$ test or Fisher's exact test if any expected cell count was <5. P-values <0.05 were considered statistically significant.

Results

Our series comprised 375 cases of IE. The mean age of patients with IE was 60±16 years. Nine patients (2%) had a PPVIE. Clinical features of patients with PPVIE are shown in Table 1. The mean time from the implant of the pulmonary valve to the diagnosis of IE was 8 years: The Melody prosthetic pulmonary valve showed a shorter time to IE than the homografts (mean 4 vs. 12 years). A comparison of the general characteristics of patients with and without PPVIE is shown in Table 2. Patients with PPVIE were significantly younger: 31 vs 60 years old (p<0.0001). At least one patient with a prosthetic pulmonary valve had a previous IE event whereas 13 patients without PPVIE had at least a previous IE event (NS). A presumed portal of entry could only be identified in 4 of the 9 patients with PPVIE. The most common was a dental origin (3 patients). The latency period between the onset of symptoms and the diagnosis of endocarditis was similar in both groups: a mean of 12 days in the PPVIE and 33 days in the non-PPVIE group. The rate of negative blood cultures and the distribution of the causative microorganism showed a similar proportion between groups (Table 2). Transthoracic echocardiography was performed in all patients. The rate of echocardiographically detected vegetations were not significantly different: 8 of 9 patients (89%) with PPVIE and 346 of 366 patients (95%) without PPVIE. Diagnosis of IE was made in 2 patients with prosthetic pulmonary valves using a PET CT imaging scan.

Table 1: Clinical features of patients with prosthetic pulmonary valve infective endocarditis

Number	Diagnosis	Age at implant	Type of prostheses	Time to IE (years)	Microorganism	Surgical findings	Outcome
1	Congenital aortic stenosis. Ross procedure	28y	Homograft	7	*S.aureus*	-	alive
2	Congenital aortic stenosis. Ross procedure	36y	Homograft	8	*S.viridans*	Stenosis	alive
3	Truncus type 1	1m	Contegra conduit	5	CNS	Degenerated heterograft	alive
4	Aortic regurgitation. Ross procedure	46y	Melody	4	Unknown	Stenosis	alive
5	d-TGA	18y	Melody	4	CNS	-	dead
6	Double outlet right ventricle	6y	Homograft	15	*S.viridans*	Abscess	dead
7	Pseudotruncus	15y	Melody	6	*S.aureus*	Stenosis	alive
8	Fallot tetralogy	13y	Homograft	11	*E.faecalis*	-	alive
9	Pseudotruncus	11y	Homograft	20	CNS	Abscess	alive

CNS: Coagulase-negative *staphylococci*

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Complications during the active phase of the disease were equally frequent in the two groups (78% in the PPVIE group and 75% in the other group). There were no differences between groups regarding heart failure, peripheral embolisms, persistent sepsis, neurological complications, abscesses, or mycotic aneurysms (Table 2).

As expected, the surgery rate during hospital admission was similar in the 2 groups. Six patients (66%) in the PPVIE group and 203 patients (56%) in the non PPVIE were operated on during the active phase. The most common indication for surgery in PPVIE was persistent sepsis (50 vs. 20%, NS) followed by the onset of congestive heart failure (33% vs. 62%, NS). Surgery was indicated as an emergency because of clinical instability or hemodynamic impairment in 1 patient (17%) with prosthetic pulmonary valve IE and in 58 patients (29%) without PPVIE (NS). Likewise, the difference in the elective surgery rate was not different (83% and 71%, respectively). Surgical findings of PPVIE patients operated on were: massive vegetations obstructing the right ventricle outflow tract (3 patients), local abscesses (2 patients), and infection confined only to the valve leaflets causing valve destruction (1 patient).

In-hospital mortality rates were also similar between the two groups (2 patients [22%] in the PPVIE group). One of these patients died because of severe complications after IE of the Melody valve implanted 4 years before due to degenerated Rastelli procedure. The infection was caused by coagulase-negative staphylococci, the patient was male and aged 24 years at the time of IE and was not operated on due to the high risk of the intervention. The infection was extended to the aortic root and tricuspid valve. In the other patient, also a 21-year-old male, a degenerated homograft implanted 15 years before, was infected. The infection was caused by viridans streptococci and he was operated on an emergency basis due to septic shock but unfortunately, the patient died. In hospital mortality of non PPVIE group was 27% (98 patients).

Table 2: Clinical characteristics of patients with and without prosthetic pulmonary valve infective endocarditis

	PPVIE (n=9)		Non PPVIE (n=366)	
Age (years) *	31±15		60±15	
Men	8	(90%)	249	(68%)
Portal of entry of infection				
Dental procedure	30	(8%)	0	(0%)
Other	144	(41%)	4	(44%)
Infective microorganism				
S. aureus	2	(22%)	71	(19%)
coagulase negative staphylococci	3	(33%)	69	(19%)
S. viridans	2	(22%)	65	(18%)
Enterococcus spp	1	(11%)	74	(20%)
Other	0	(0%)	32	(9%)
Unknown	1	(11%)	60	(16%)
Complications				
Heart failure	5	(56%)	198	(54%)
Persistent sepsis	4	(44%)	77	(21%)
Surgical treatment				
Urgent	1	(11%)	58	(16%)
Elective	5	(56%)	145	(40%)
In hospital mortality	2	(22%)	98	(27%)

*p<0.001

All patients were prospectively followed up for a mean period of 26±32 months in the PPVIE group and 39±49 months in the non-PPVIE group (NS). No patients were lost to follow-up. No recurrence of endocarditis occurred in patients with PPVIE. None of the seven survivors with PPVIE to the active phase were operated on nor died during follow-up.

Discussion

Prosthetic valve endocarditis is a serious life-threatening condition with a mortality of up to 20% [1]. Usually, left-side prosthetic valve IE has a poorer prognosis compared to right-side prosthetic valve IE, mostly related to local complications such as penannular abscess, embolic events, and heart failure [1,2]. In cases of IE affecting prosthetic pulmonary valves, although patients are younger, they are at higher risk as they usually have a congenital heart disease treated previously with one o more surgical interventions and sometimes applies to young patients that will require more heart operations during their lives. For such reason, the ideal therapeutic strategy is debatable and varies between a conservative approach of antibiotic treatment only and surgical removal of all infected tissue. As expected, our patients with PPVIE were young (mean age 31±15 years old) and similar to previously reported [2,3,7,8].

Our study shows that the incidence of PPVIE in a tertiary hospital is as low as previously reported and similar to that reported by the Euro Endo Registry (2.4%) [1]. Due to its low incidence, information on clinical features of patients with PPVIE comes from a few nationwide registries [3,4], prospective valve trials sponsored by valve companies [7], or single center experience [2,8].

According to a recent German registry [3], homografts had the lowest incidence of pulmonary valve-related IE, and Melody valves had the highest. However, no clear potential factor for the increased risk of IE for the Melody valve has been identified so far. Although we can not assess the incidence of IE in patients with pulmonary prostheses valve, the mean time from prostheses implant to IE was shorter among patients with Melody valves than homograft. We hypothesize that Melody valves degenerate earlier than homograft and cause more severe right ventricle outflow tract (RVOT) obstruction during follow-up. Some authors have associated RVOT stenosis with higher endocarditis risk [9]

Diagnosis of right side IE is often delayed, since subtle symptoms, rather than systemic signs of IE predominate. A variety of complications caused by septic pulmonary emboli have been described, such as pulmonary infarction, pulmonary abscesses, bilateral pneumothoraces, pleural effusions, and empyema [1]. It is noteworthy that up to 20% of patients with

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PPVIE are operated on due to stenosis caused by vegetation [10,12]. In our series, 2 of 8 PPVIE patients were operated on due to stenosis and severe obstruction of RVOT. Most PPVIE patients suffered severe complications during the active phase, mainly persistent sepsis and heart failure leading both complications to surgery during hospitalization. Weber *et al* [2] reported a longer time between diagnosis and operation of right side IE compared to left side IE. In our series, the mean time from onset symptoms to diagnosis was similar to other types of IE as was the interval time to surgery from admission to hospital (42±19 days vs 53±14 days).

Staphylococci were the most common causative microorganisms in our cohort of PPVIE. This finding is consistent with previous studies [3,9,10] reporting a 43% incidence of *staphylococcus aureus* infection, followed by coagulase-negative staphylococci and *enterococcus faecalis*. All these microorganisms are considered risk factors for mortality [10-12].

Datar *et al* report a surgical mortality rate of 5.5%, which should be considered low in an IE population [4]. Other small series report mortality rates ranging from 0% to 15% [7,8]. This low in-hospital mortality rate is lower than that at our institution (16.6%) and may reflect different patient profiles with more advanced congenital heart disease with often a homograft previously degenerated. Several risk factors for mortality in right side IE have been described, including the type of causative microorganisms, large vegetations, and patients with a redo intervention [2]. Antibiotic penetration is impaired in these patients complicating the eradication of even less aggressive organisms.

Our study has several limitations that need to be considered for the interpretation of the results. First, this is a single-center study with retrospectively collected data for a very limited number of patients. Like other reports, it is an observational study of patients from a tertiary institution with a special interest in IE with a cardiac surgical program. Second, referral bias in these studies is common thus information concerning patients not transferred to our hospital is missing. And last, the number of patients with PPVIE is very small therefore larger multicentre studies addressing the such issue should be desirable.

In summary, PPVIE affects young patients often with multiple redo interventions and clinical outcomes are similar to other types of IE. With similar complication rates during the active phase, cardiac surgery performance and in-hospital mortality are similar to those with non-PPVIE.

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