

Valve selection in aortic valve endocarditis

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Abstract

Aortic prosthetic valve endocarditis (PVE) is a potentially life-threatening disease. Mortality and incidence of infective endocarditis have been reduced in the past 30 years. Medical treatment of aortic PVE may be successful in patients who have a prompt response after antibiotic treatment and who do not have prosthetic dysfunction. In advanced stages, antibiotic therapy alone is insufficient to control the disease, and surgical intervention is necessary. Surgical treatment may be lifesaving, but it is still associated with considerable morbidity and mortality. The aim of surgery is to perform a radical excision of all infected and necrotic tissue, reconstruction of the left ventricle outflow tract, and replacement of the aortic valve. There is no unanimous consensus on which is the optimal prosthesis to implant in this context, and several surgical techniques have been suggested. We aim to analyze the efficacy of the surgical treatment and discuss the issue of valve selection in patients with aortic valve endocarditis.

Key words: aortic valve endocarditis, surgery, infective endocarditis.

Streszczenie

Zapalenie wsierdza na sztucznej zastawce aortalnej (PVE) jest chorobą zagrażającą życiu pacjenta. Wskaźniki śmiertelności i zapadalności infekcyjnego zapalenia wsierdza zmniejszyły się w ciągu ostatnich 30 lat. Terapia aortalnego PVE może być skuteczna u pacjentów bez dysfunkcji protezy, u których następuje szybka odpowiedź na antybiotykoterapię. W zaawansowanym stadium choroby antybiotykoterapia nie wystarcza do jej opanowania i potrzebna jest interwencja chirurgiczna. Leczenie chirurgiczne może uratować życie pacjenta, jednak wiąże się ze znaczną chorobowością i śmiertelnością. Celem chirurgii jest wykonanie radykalnego wycięcia całej zainfekowanej i nekrotycznej tkanki, rekonstrukcja drogi odpływu lewej komory oraz wymiana zastawki aortalnej. Nie ma konsensusu dotyczącego optymalnej protezy, którą należałoby wszczepić w takiej sytuacji; sugeruje się też stosowanie kilku technik chirurgicznych. Naszym celem była analiza skuteczności leczenia chirurgicznego oraz omówienie doboru zastawki u pacjentów z zapaleniem wsierdza na zastawce aortalnej.

Słowa kluczowe: zapalenie wsierdza na zastawce aortalnej, chirurgia, infekcyjne zapalenie wsierdza.

Introduction

Prosthetic aortic valves are a risk factor for infective endocarditis (IE), and prosthetic valve endocarditis (PVE) remains potentially a life-threatening disease. Prosthetic valve endocarditis can be diagnosed in about 1% to 6% of patients with valve prostheses [1]. In selected cases, cure by medical treatment can be achieved in patients with PVE [2]. Patients diagnosed early in the course of the disease, patients with a prompt antibiotic response or with streptococcal disease, and patients with echocardiographic findings such as small or absent vegetations, no severe prosthetic dysfunction, and no periprosthetic tissue damage, are candidates for conservative management.

In advanced stages, however, antibiotic therapy alone is insufficient to control the disease [3], and surgical intervention is necessary. Surgery is required in patients with heart failure or cardiogenic shock caused by valvular dysfunction.

Surgery should also be undertaken in hemodynamically stable patients with abscess, recurrent emboli despite appropriate antibiotic therapy, aggressive infection resistant to antibiotic therapy, and fungal endocarditis [4]. Surgical therapy involves excision of all infected and necrotic tissue, drainage of abscesses, closure of fistulas, and complete removal of prosthetic material, replacement of the aortic valve and reconstruction or replacement of the aortic root. The surgical operation extends from only removal and replacement of the infected aortic prostheses to a more complex situation with radical resection and replacement of the aortic root, the outflow tract, and even the ascending aorta. Even with aggressive surgical therapy, the infection may be difficult to eradicate, and mortality and morbidity remain high [4]. The optimal type of aortic prosthesis for patients with PVE remains unclear; different prosthetic valves are used and different surgical techniques are applied in this group of patients [5–15].

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In this article, we analyzed, through a literature review, the efficacy of the surgical treatment and the issue of valve selection in patients with aortic valve endocarditis.

Material and methods

Literature search

A computerized search of the English-published literature was conducted on the Medline database. The selected articles were reviewed by the authors and judged on their relevant contribution to the subject of this study.

Search strategy

The literature was reviewed primarily by searching the Medline database from 1946 to November 2013 using the OVID interface (*Endocarditis/di, su, th OR aortic valve endocarditis.mp. OR prosthetic aortic valve endocarditis.mp.)

Search outcome

The following steps were performed: identification of titles through a database search, removal of duplicates, screening of abstracts, assessment of full-text articles for eligibility, and final inclusion in the study. A total of 1479 reports were found in the Medline database, of which 40 were included in this review.

Inclusion criteria

Studies concerning aortic PVE were selected for analysis. The inclusion criteria were: full text papers that reported the surgical treatment, the post-operative mortality, need for reoperation due to reinfection, midterm or long-term follow-up.

Discussion

Endocarditis of a native aortic valve, and especially of a prosthetic aortic valve, is an uncommon disease with an incidence of 0.3–1.2% per patient per year, while the prevalence varies in different studies between 1% and 6% [1]. A limited extent of retrospective and very few prospective reports are published in the literature, and a comparison of the outcomes is difficult because most series contain heterogeneous patient populations: patients with both prosthetic and native valve endocarditis, both mitral and aortic valve endocarditis, and both healed and active endocarditis. Often, the patients are collected over a long period of time and were operated on by several surgeons through different surgical techniques; sometimes the patients are from several hospitals. These factors could present a limitation in making a definitive judgment on this specific clinical scenario.

Pathophysiology

Prosthetic valve endocarditis represents 10–30% of cases of IE in most developed countries [4]. The risk of early-onset endocarditis is greater for mechanical heart valves, but later after implantation, the incidence becomes similar for mechanical prostheses and bioprostheses [4]. Gram-

positive organisms are the main etiologic agents in endocarditis of the aortic valve. Microorganisms of the genus *Streptococcus* are primarily detected in cases of native aortic valve endocarditis [5, 10], whereas agents of the genus *Staphylococcus* are identified in patients with PVE [5, 10] and are associated with a poor prognosis [4]. *Staphylococcus* has the ability to adhere on prosthetic devices, start biofilm production, and secrete exoenzymes [16]. Once attachment of the bacteria has been achieved, an extracellular polysaccharide matrix is produced, which engulfs the bacteria and then works as a barrier to antibacterial access and may inhibit host defenses [16].

Graft selection in aortic valve endocarditis

The optimal type of aortic prosthesis for patients with IE remains unclear. The general consensus clearly tends toward the use of biological material rather than prosthetic devices for surgical repair in the presence of infection [5, 6, 17].

Aortic homograft

Many authors consider the aortic homograft as the gold standard in the treatment of aortic valve endocarditis. Several reports have suggested the use of an aortic homograft in IE [5, 6, 17–23] (Tab. I). Sabik *et al.* [6] and Musci *et al.* [20] reported on the largest series of patients with PVE who have undergone homograft implantation, while the majority of the authors reported on much smaller series of patients and included both patients with native and those with prosthetic valve endocarditis. The reported 30-day mortality ranges between 3.9% and 25% in patients with PVE [6, 20] and 3% and 16% in patients with native valve endocarditis (NVE) [19, 20], showing a better outcome for patients with NVE. In addition, the survival at 1, 5 and 10 years is better for patients operated on for NVE than for those with PVE [5, 20], indicating that patients with PVE have worse survival than those with native endocarditis.

Long-term survival at 1 year in patients with PVE ranges between 67% and 92% [20, 21]. However, if we look at those authors who report only on PVE, 1-year survival is better, ranging from 81% to 92% [21, 23]. The same difference can be observed for the survival at 5 years, which ranges from 48% to 85% [20, 22] in mixed series, while it ranges from 70% to 85% [5, 22] in selected series. Late mortality is not due to recurrent infection or valve dysfunction, but it seemed to be related to the patients' bad clinical condition.

The reinfection incidence in aortic homograft replacement is low, ranging from 0 to 6.8% in the majority of the studies [5, 6, 20, 24], but higher incidence has been reported [25]. Some studies report a higher incidence of recurrent endocarditis in patients treated with mechanical or biological valve prostheses than in patients treated with a homograft [24], while other authors report no difference in the rate of recurrent infection between patients who received a homograft and those who received a conventional prosthesis [10, 25, 26]. The low incidence of early and late recurrent infection reported is mainly the result of early diagnosis, aggressive surgical management, including com-

Tab. I. Outcome of patients with aortic valve endocarditis treated with implantation of an aortic homograft

Author	Total patients	Patients treated with AH	30-day mortality (%)	Reinfection (%)	SVD (%)	Survival (%)		
						1 year	5 years	10 years
Perrotta 2015	87 PVE	56	10.7	None	5.3	NA	74%	58%
Perrotta 2010	62	62	15	1.6	1.6	82	75	67
	31 NVE		10			88	79	79
	31 PVE		19			78	70	51
Musci 2010	221	221	21	5.4	8.6	77	66	47
	99 NVE		16	6	11		66	47
	122 PVE		25	4.9	6.5		67	48
Lopes 2007	41 PVE	41	4.9	None	4.8	91	85	79
Grinda 2005	104	104	5	5.7	5.7	93	86	83
	76 NVE		3					
	28 PVE		11					
Yankah 2005	161	161	14	6.8	1.2	75	70	70
	80 NVE							
	81 PVE							
Leyh 2004	29 PVE	16	18.7	None	None	81	81	NA
Sabik 2002	103 PVE	103	3.9	3.8	NA	90	73	56
Lytle 2002	27 PVE	27	4	4	NA	92	70	NA
Niwaya 1999	81	46	17	2.1	None	NA	69	NA
	52 NVE							
	29 PVE							

AH – aortic homograft, NA – not available, NVE – native valve endocarditis, PVE – prosthetic valve endocarditis, SVD – structural valve deterioration

plete resection of all infected tissue, adequate antibiotic treatment, and liberal use of aortic homografts.

Homografts deteriorate progressively and may necessitate reoperation [20]. It has been demonstrated, mainly in patients without endocarditis, that the risk of dysfunction is substantial and higher for homografts than for unstented biological valves [27]. The incidence of structural valve deterioration in patients with IE ranges from 2% to 8.6% [5, 20, 24]. However, it should be pointed out that the number of patients who underwent reoperation only reflects the most severe forms of deterioration. Some patients may have severe deterioration of the homograft but are not reoperated on due to their general condition, comorbidity, or age.

However, although homografts may confer a theoretical advantage in resisting infection because of their lack of artificial materials [6], their use is accompanied by a number of potential drawbacks. Homografts have a limited availability and deteriorate progressively once implanted, ensuring that reoperation will eventually be required, and the presence of severe adhesions will make such reoperations technically challenging. Moreover, an irregular base for the proximal suture line can distort a homograft and render it insufficient.

Stentless prosthesis

Aortic homografts are not always readily available; thus, several authors have suggested the use of stentless prostheses in this clinical scenario. In 2008 Musci *et al.* [7] reported on the largest series of Dacron-free stentless

prostheses implanted in 255 patients with both native and prosthetic aortic endocarditis. He reported an overall reinfection rate of 8.6%, with 83% freedom from reinfection at 5 years and 5-year survival of 46%. Furthermore, he did not find a statistically significant difference in survival and freedom from reinfection between patients with NVE and those with PVE ($p = 0.14$ and $p = 0.84$). In 2010, in a series of 221 patients treated with an aortic homograft, the same author [20] reported a reinfection rate of 5.4% and 10-year freedom from reoperation and reinfection of 92% in native and PVE cases. Long-term survival, at 10 years, was better in native than in PVE ($p = 0.029$).

Stentless prostheses seem to offer low reinfection rates, ranging from 3.7% to 8.6% [7, 28]. The low reinfection rates and good hemodynamic values are comparable to those of cryopreserved homografts. The required stentless prosthesis is available at any time and in several sizes, and its specific design allows the application of a variety of surgical techniques. In patients with less extensive aortic root abscess, these valves can be implanted in the subcoronary position, whereas in patients with a more extensive infection, in which the abscess is localized at and above the level of the annulus, the bioprosthesis can be inserted as a total root replacement [8].

Selection of valve substitute

There is no unanimous consensus regarding the use of aortic homografts and stentless prostheses, and whether or not such prostheses provide incremental benefits over the use of standard prostheses. The issue of graft selection

in prosthetic and native aortic valve endocarditis has been debated by some authors who have compared the results of patients with IE treated with implantation of an aortic homograft or standard prosthesis [17, 24–26, 29–31] (Tab. II).

The 30-day mortality reported in the literature ranges from 6.7% to 17% for patients who were treated with an aortic homograft [17, 29] and from 3% to 23.5% for those who received conventional prostheses [26, 31]. Long-term survival between the two groups, at 1, 5 and 10 years, does not show significant differences, suggesting that factors other than the prosthetic devices are associated with late mortality. The reinfection rate, in patients with aortic homograft, ranges between 0 and 7% in the majority of studies [17, 24–26, 30, 31], but higher incidence has been reported [29]. In patients treated with standard prostheses, the incidence of recurrent endocarditis is reported to be generally higher than in patients treated with a homograft [31]. However, a high reinfection rate is reported in both groups [29, 31]. These data were confirmed by Moon *et al.* [10], who in a large series of 306 patients with left-sided endocarditis reported no significant difference in operative mortality regardless of whether a mechanical, bioprosthetic, or homograft valve was selected ($p > 0.74$), and the overall long-term survival rates were also similar at both 10 years and 20 years ($p > 0.27$). The author could not identify any difference in rate of recurrent or residual endocarditis among the three groups; during the first 5 years it was $2.1 \pm 1.1\%$ per patient-year in the mechanical valve cohort, $2.3 \pm 0.6\%$ in those with bioprostheses, and $3.6 \pm 2.5\%$ in the homograft valve recipients ($p > 0.88$ between groups). It seems that the material, biological versus prosthetic, used for aortic root replacement has no effect on hospital mortality, long-term mortal-

ity, or the incidence of recurrent PVE. The implantation of conventional material, when technically feasible, provides a good solution for patients with no anticoagulation contraindications and is associated with a similar outcome to aortic homograft implantation. However, a homograft valve is ideally suited for reconstruction of the aortic root in the presence of an abscess, because it is easier to handle than conventional prostheses and its anterior mitral leaflet can be used to patch the defect created by the resection of the abscess [32]. The type of prosthesis to be implanted should be selected on the basis of the complete clinical picture for a given patient and the availability and hemodynamic performance of a conduit of the appropriate size.

In case of severe destruction of the aortic annulus, a prosthetic material can be used with the condition that the infected area is carefully debrided and the prosthesis is distanced from the focus of the infection; thus, the “translocation” of the valve prosthesis in an aortic tube seems to be a surgical option in these particular settings [33], and in extreme cases heart transplantation can be taken into consideration [34].

Use of composite graft in infective endocarditis

A mechanical or biological composite graft is an alternative option in patients with extensive root destruction [12, 13, 23] (Tab. III). In the literature, there are a few articles that report the use of composite grafts in aortic PVE [12, 13, 23]. These authors reported on a limited number of patients with complex aortic PVE who had undergone either Bentall surgery or the Cabrol procedure. They reported 30-day mortality between 11% and 15%, recurrence of infec-

Tab. II. Outcome of patients with aortic valve endocarditis treated with implantation of an aortic homograft or conventional prostheses

Author	Total patients	Valve implanted	30-day mortality (%)	Abscess (%)	SVD (%)	Reinfection (%)	Survival (%)		
							1 year	5 years	10 years
Perrotta 2015	87 PVE	AH 56	10.7	NA	5.3	None	NA	74	58
		CP 31	9.7	NA	NA		NA	87	75
Jassar 2011	134	AH 36	6.7	78	NA	17	61	58	NA
	44 NVE	BP 55	9.7	84	NA	5	65	62	NA
	90 PVE	MP 43	5.9	84	NA	12	67	58	NA
Leontyev 2011	172	AH 13	NA	NA	NA	None	100	100	NA
	96 NVE	BP 141	NA	NA	NA	NA	85	76	NA
	76 PVE	MP 18	NA	NA	NA	NA	88	84	NA
Klieverik 2009	138 NVE	AH 106	9	38	4.7	6	90	80	69
		MP 32	3	19	3	93	85	74	
Avierinos 2007	127	AH 54	11	75	NA	7	86	80	43
	88 NVE	CP 73	8	30	7	5	79	54	54
	39 PVE								
Knosalla 2000	65	AH 47	8.5	94	6	2	89	82	82
	NVE 47	CP 18	23.5	83	None	17	65	65	65
	PVE 18								
Niwaya 1999	81	AH 46	17	NA	NA	2	NA	69	NA
	52 NVE	Ross 25	12	NA	NA	4	NA	88	NA
	29 PVE	CP 10	20	NA	NA	10	NA	29	NA

AH – aortic homograft, BP – biological prostheses, CP – conventional prostheses, MP – mechanical prostheses, NA – not available, NVE – native valve endocarditis, PVE – prosthetic valve endocarditis, SVD – structural valve deterioration

Tab. III. Outcome of patients with aortic valve endocarditis treated with implantation of mechanical or biological composite graft

Author	Total patients	Patients treated with composite	30-day mortality (%)	Reinfection (%)	Survival (%)		
					1 year	5 years	10 years
Wilbring 2012	31 PVE	31	12.3	None	80	75	NA
Leyh 2004	29 PVE	13	15	None	85	85	NA
Hagl 2002	28 PVE	28	11	4	81	81	NA

NA – not available, PVE – prosthetic valve endocarditis

tion between 0 and 4%, and 5-year survival between 75% and 85%. In selected centers, this surgical approach seems to be feasible, and the results are comparable with those from the use of the aortic homograft.

Ross operation in infective endocarditis

The use of the Ross procedure for the treatment of aortic valve endocarditis has been suggested by some authors [35, 36]. However, few series specifically report the results of the Ross procedure in aortic native and prosthetic endocarditis. The number of patients treated in these series is limited, and often the data are recorded over several years. The reported hospital mortality ranges from 4.7% to 12% [17, 36] and the 5-year survival ranges from 93% to 88% [17, 36]. In a recent study [36], the author reported a reinfection rate of 7% and pulmonary artery stenosis rate of 19% after a medium follow-up of 10 years. The Ross procedure seems to be feasible and can be safely performed with good mid-term results, and it can be considered an alternative to the aortic homograft and prosthetic valves. Due to the limited number of patients treated and the short follow-up, the final judgment of the pulmonary autograft in patients with aortic valve endocarditis remains inconclusive.

The primary motivation for using a Ross operation for patients with aortic endocarditis is to provide a prosthesis that does not require anticoagulation, which have a low risk of re-infection, have good hemodynamic performances and will have a chance of being a permanent solution due to its potential of growth. There is strong criticism of the Ross operation because this surgical technique consists of a double valve replacement for a single valve disease, requires longer cross clamp times, and similar results can be achieved using an aortic homograft. The technique has the risk of development of a homograft stenosis in the right ventricular outflow tract that is inherent in the Ross procedure, and it is considered to be a technically challenging procedure and should be performed by surgeons familiar with the technique.

Eradication of the infection

Prosthetic infectious endocarditis is a progressive and continuous disease, and its action results in progressive periannular destruction with abscess formation, valve dehiscence, and, consequently, hemodynamic deterioration. Once the diagnosis of aortic valve endocarditis has been

established and there is an indication for surgical intervention, surgery should not be delayed [10, 13, 23]. The key to success in the treatment of the disease is radical debridement with resection of all infectious and necrotic tissue, regardless of the cardiac structures involved [32], and prolonged antibiotic therapy [4].

Surgery of the abscess

The extension to the paravalvular tissue represents the natural evolution of the infection of the valvular cusps in the case of a native valve, or the prosthetic ring in the case of a pre-existing prosthesis. The degree of para-annular involvement is closely linked to the virulence of the microorganism and to the duration of the infection before antibiotic treatment. This condition can lead to valve dehiscence, aortic-to-atrial fistula, left fibrous trigone abscess, or ventricular septal defect.

The ideal surgical treatment of active endocarditis aims to debride the infected tissue regardless of the proximity of the conduction system, to exclude the abscess cavity from the circulation and subsequently from the prosthesis, eliminate all the possible foci of infection, and reconstruct the aortic annulus and the left ventricle outflow tract.

Small annular abscess cavities without perforation into other cardiac chambers can be debrided and filled with antibiotic-impregnated fibrin glue or simply incorporated into the valve fixation sutures [37]. It is reported that fibrin-glue-sealed defects may withstand high burst pressure, but it failed to obliterate perfused cavities in the dead space between the native aortic and the allograft aortic wall [38]. An abscess limited to the aortic annulus and not perforating the aortic wall can be removed by excision of that portion of the annulus and corresponding aortic wall, and the reconstruction of the annulus can be performed with a tailored patch of autologous pericardium [39]. A more extensive resection is needed when the abscess extends through the aortic wall into other tissues or cavities. When the interventricular septum is involved, a radical resection of the infected tissues is performed regardless of the proximity of the conduction system, and the reconstruction can be performed with an autologous pericardial patch. In the presence of mitro-aortic infection with destruction of the left fibrous trigone extension, a complete mitro-aortic monobloc replacement can be performed [40].

Study limitations

The most important limitations of this review are the retrospective study design of the articles analyzed and the limited number of patients included. The retrospective design implies inevitable selection bias, and the limited number of patients implies a pronounced risk for statistical type II errors. The patients were collected over a long period. The diagnostic preoperative assessment of patients with IE differed in the articles, and the patients underwent different surgical techniques performed by different surgeons. Another limitation is that comorbidities, such as stroke and heart failure, may influence the results.

Conclusions

In aortic valve endocarditis, early surgery should be considered. There is no clear evidence on which is the most appropriate valve substitute in infective endocarditis. The low rate of recurrence of infection is mainly attributed to radical debridement and resection of all infected tissue and prolonged antibiotic therapy. Patients with extreme aortic root destruction and with an aortic root abscess can be more easily treated by implantation of an aortic homograft. Stentless prostheses can be valid alternatives to homografts. However, most anatomic lesions can be treated by annulus reconstruction and aortic root replacement with conventional prostheses. All these devices provide a good solution in terms of survival and recurrent endocarditis. The use of a composite graft is feasible, with results comparable to those of aortic homograft root replacement; however, the procedure is associated with high mortality and morbidity. The Ross procedure seems to be a feasible surgical option, but the limited number of patients treated makes it difficult to give a definitive judgment on its validity. The type of prosthetic device to implant should be selected on the basis of the complete clinical picture for a given patient, including the technical requirements for reconstruction, the patient's age and comorbidities, an assessment of compliance with medication and follow-up, and the availability and hemodynamic performance of a conduit of the appropriate size.

Disclosure

Authors report no conflict of interest.

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