Prosthetic valve endocarditis

A survey

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SUMMARY Fifty eight patients (aged 8-59 years, mean 27) treated for prosthetic valve endocarditis from January 1966 to January 1985 were studied retrospectively by review of case notes. There were 12 cases of early and 46 cases of late prosthetic valve endocarditis. These developed in 28 patients with an isolated aortic valve, in 26 with an isolated mitral valve, and in four with both aortic and mitral prosthetic valves. Streptococci were the most commonly isolated micro-organisms, followed by staphylococci, Gram negative bacteria, and fungi. A surgical (34 cases) or a necropsy specimen (10 cases) from 44 cases was examined. Eighty two per cent of the patients had congestive heart failure. Twenty four of the 58 patients were medically treated and 17 died (70% mortality). Combined medical and surgical treatment was used in 34 patients; the main indication for surgery was congestive heart failure. Fourteen patients on combined treatment died (40% mortality). Persistent sepsis and prosthetic valve dehiscence were the most common early and late operative complications. The most important influences on outcome were congestive heart failure, the type of micro-organism, the severity and extent of anatomical lesions, the time of onset of prosthetic valve endocarditis, and the type of treatment.

This survey indicates that only patients without congestive heart failure or embolic complications and with sensitive micro-organism should be treated medically. In view of the poor prognosis patients with prosthetic valve endocarditis associated with congestive heart failure, persistent sepsis, and repeat arterial emboli should be treated by early surgical intervention.

Despite advances in antimicrobial treatment and in surgical management, postoperative endocarditis still causes considerable morbidity and mortality in patients with prosthetic heart valves. We examined the clinical course and treatment of 58 patients with prosthetic valves who presented with endocarditis over a 15 year period (1968-84).

Patients and methods

Patients treated for prosthetic valve endocarditis from January 1966 to December 1984 were studied retrospectively by review of case notes.

The diagnosis of prosthetic valve endocarditis was established by the presence of one or both of the following criteria: histopathological evidence of endocarditis in a surgical or necropsy specimen; at

least two blood cultures that were positive for the same organism and associated with an obvious clinical picture of prosthetic valve endocarditis, valve dysfunction, or signs of septic emboli. Endocarditis diagnosed within 60 days of operation was classified as early, cases presenting beyond this time were classified as late endocarditis. The term active prosthetic valve endocarditis included patients with positive blood cultures in the 48 hours before surgical intervention, a prosthesis giving a positive culture, or a myocardial abscess found at operation or necropsy. We used the χ^2 test for statistical analysis.

Results

Prosthetic valve endocarditis developed in 58 (5.9%) (38 M, 24 F) of 979 patients with cardiac valve replacement followed by us at our hospital between January 1968 and December 1984. The age range of these 58 patients was 8-59 years (mean 27 years). There were 12 cases of early and 46 of late

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prosthetic valve endocarditis. Endocarditis developed in 28 patients with an aortic valve, in 26 with a mitral valve, and in four with combined aortic and mitral valve replacement.

CLINICAL CHARACTERISTICS

Fever was the most common clinical finding (55 (95%)). Other physical signs were splenomegaly (10 (17%)) and cutaneous signs (11 (18%)). Anaemia, with haematocrit of <35% and increased white cell count was detected in 50%; 28% had haematuria and 16% had proteinuria. Nearly all the patients had an increased erythrocyte sedimentation rate.

MICROBIOLOGY

Table 1 shows the micro-organisms that caused prosthetic valve endocarditis in this study. These were identified by blood cultures from 34 (59%) patients. Streptococci were the most commonly isolated organism, followed by staphylococci, Gram negative bacteria, and fungi. Twenty four (41%) patients had negative blood cultures. Streptococci were more common in late prosthetic valve endocarditis, whereas more antibiotic resistant micro-organisms (staphylococci, Gram negative bacteria) were more common in early prosthetic valve endocarditis. Table 2 shows the likely sources of infection in 36 (62%) patients. Portals of entry were different in early and late prosthetic valve endocarditis; in late prosthetic valve endocarditis dental treatment (usually without antibiotic prophylaxis) was the most common factor identified, followed by genital and urinary tract infection. Infections causing early prosthetic valve endocarditis occurred mainly during cardiopulmonary bypass or in the early post-operative period (11/12 cases). Immunological investigations were performed in only four patients.

ECHOCARDIOGRAPHY

Echocardiography was performed in 18 patients.

Table 1 Microbiological causes of prosthetic valve endocarditis (PVE) in 58 patients (12 early cases and 46 late cases)

Micro-organism	No of patients		
	Early PVE (12)	Late PVE (46)	Total (58)
Streptococcus	1	13	14 (24%)
Staphylococcus			
<i>S. epidermidis</i>	2	3	5 (9%)
<i>S. aureus</i>	2	3	5 (9%)
Gram negative bacteria	2	7	9 (15.5%)
<i>Candida albicans</i>	0	1	1 (1.7%)
Negative blood culture	5	19	24 (41%)

Dehiscence of the prosthetic device was seen in two patients with aortic valve replacement and vegetations in three patients also with prosthetic aortic valves.

PATHOLOGICAL CHANGES

Examination of surgical (34 cases) or necropsy specimens (10 cases) found abnormalities in 26 aortic and 21 mitral prostheses (table 3). The most common lesions were dehiscence (36/44) and vegetations (33/44); thromboses were more common on mitral prostheses than on aortic prostheses. The valve ring was usually considerably altered and extension of the infection to the adjacent cardiac structures was common. In the three bioprostheses that were examined infection affected the valve leaflets but not adjacent host tissue.

COMPLICATIONS

Congestive heart failure occurred in 48 patients (82%) (12 early and 36 late cases of prosthetic valve endocarditis), neurological complications in 15 (25%) (13 embolic strokes and two cerebral abscesses) (three early and 12 late cases of prosthetic valve endocarditis), and peripheral vascular emboli in 27 patients (46%) (three early and 24 late cases of prosthetic valve endocarditis).

Fever persisted in 21 patients (nine early and 12 late prosthetic valve endocarditis) after the start of appropriate medical treatment, and atrioventricular conduction disturbances with complete heart block, related to extension of the infection to the conduction system, were seen in three patients with late prosthetic valve endocarditis; six (10%) patients with prosthetic valve endocarditis (all late cases) had renal failure.

TREATMENT AND OUTCOME

Twenty four patients had medical treatment alone; seven survived. Thirty four patients had combined medical and surgical treatment (table 4). Twenty three patients were operated on in France and 11 in Tunis.

Table 2 Sources of infection in 36 patients with prosthetic valve endocarditis (PVE)

Portal of entry	Early PVE	Late PVE	Total
Dental treatment	1	6	7
Cutaneous infection		1	1
Urinary tract infection		4	4
Pulmonary infection		4	4
Genital infection		5	5
Gastric infection		2	2
Caesarean section		1	1
Post-cardiopulmonary bypass	11		11

Table 3 Pathological findings in 26 aortic and 21 mitral prostheses or bioprostheses seen at operation (34 cases) or at necropsy (10 cases)

Finding	Aortic replacement (26)	Mitral replacement (21)	Total (44)	%
Valve dehiscence	20	16	36	82
Vegetations	18	15	33	75
Thrombosis	2	9	11	25
Ring valve abscess	12	4	16	36
Complete destruction of ring valve	2	1	3	7
Aortic aneurysm	4	—	4	9
Myocardial abscess	2	1	3	7
Septal involvement	2	1	3	7
Aortic abscess	1	—	1	2
Torn valve leaflets*	2	1	3	7
Extension of infection to adjacent cardiac structures	16	7	23	

*Bioprostheses.

RESULTS OF MEDICAL TREATMENT

Of the seven patients who survived after medical treatment (one with early prosthetic valve endocarditis and six with late prosthetic valve endocarditis), two were lost to follow up and five were followed for 6–120 months (mean 64 months); all of them are alive and well—one is in grade I and four in grade II of the New York Heart Association classification. The patients were not treated surgically because they responded well to medical treatment and had no obvious signs of cardiac failure or valve dysfunction. Seventeen (70%) of the medically treated patients died. We attribute this high mortality to the fact that patients treated medically were usually referred from other hospitals, they were already critically ill, with congestive heart failure, low cardiac output, and sometimes neurological disturbances, and were too ill to undergo operation. The main cause of death was prosthetic valve dys-

function or cardiac failure or both in 11 patients; neurological complications with coma was the cause of death in five patients; and persistent sepsis in one patient.

RESULTS OF COMBINED MEDICAL AND SURGICAL TREATMENT

Thirty four of the 58 patients underwent repeat operation because of prosthetic valve endocarditis, and in some instances further operations were required. Thirty had late prosthetic valve endocarditis and four had early prosthetic valve endocarditis. Fifteen were operated on during an active stage. Table 5 lists the indications for operation in patients with infected prosthetic valves.

The main indication for surgery was progressive severe congestive heart failure caused by valve dysfunction, with or without persistent sepsis. One patient with *Candida albicans* infection of a Björk mitral valve died postoperatively of low cardiac output. In all cases operation included debridement of infected tissue. In four partial valve dehiscence was repaired without valve replacement; in 30 cases, correction of a haemodynamically important paravalvar leak had to be done by valve replacement, with reconstruction of aortic annulus in six cases, supra-annular insertion of aortic prosthesis associated with coronary bypass in two cases, and insertion of a mitral prosthesis inside the atrial cavity in two cases.

Table 4 Outcome in 58 patients with prosthetic valve endocarditis

Treatment	Total No (%)	Survived No (%)	Died No (%)
Medical/antibiotics alone	24 (42)	7 (29)	17 (71)
Medical and surgical (antibiotics + reoperation)	34 (58)	20 (59)	14 (41)
Total	58	27	31

Table 5 Indications for surgical treatment of infected prosthetic valves

Indications	No patients	%
Cardiac failure (prosthetic dysfunction)	19	56
Cardiac failure and persistent sepsis	14	41
Fungal PVE	1	3

PVE, prosthetic valve endocarditis.

OPERATIVE MORTALITY

Fourteen (41%) patients died: nine from low cardiac output, three from neurological complications, one from severe septicaemia, and one from ventricular arrhythmias.

Many of the 20 patients who survived had early postoperative complications (table 6). The most frequent were persistent sepsis (5) and early prosthetic valve dehiscence (6) (three because of infection and three mechanical failures); three had a repeat valve replacement—one survived and two died. There

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Table 6 Early postoperative complications in 20 survivors two months after operation for prosthetic valve endocarditis (PVE)

Complications	No patients	%
Persistent sepsis:	5	
<i>Staphylococcus</i>	2	
Gram negative bacteria	1	25%
<i>Candida albicans</i>	1	
Negative blood culture	1	
Early prosthetic valve dehiscence	6*	
Infection	3	
Mechanical	3	30%
Cerebral emboli	2	
Ventricular arrhythmia	2	
Complete heart block	2	35%
Mediastinal infection	1	

*Three recurrent valve replacement, two deaths, and one survivor.

were two types of major complications in the 18 patients who survived for more than two months after operation: persistent sepsis (3) (two survived and one died after repeat prosthetic valve replacement because of major valve dehiscence) and late prosthetic or periprosthetic leak (6) (two minor and four major requiring subsequent reoperation with three deaths from low cardiac output).

So 14 are alive after operation. Eleven were followed (six with aortic and five with mitral valve replacement) (table 7).

Table 7 Clinical results in 11 survivors after surgical treatment for prosthetic valve endocarditis. Follow up period 18–62 months (mean 41 months)

Result	NYHA grade	CTR	ECG	Aortic (6)	Mitral (5)
Excellent	I–II	Normal	Normal		1
Good	I–II	Increased	Moderately altered	6	4

CTR, cardiothoracic ratio; NYHA, New York Heart Association.

Table 8 χ^2 test to compare mortality and survival associated with various prognostic features

	Survivors (16)	Deaths (37)	χ^2 test
PVE with congestive heart failure	8	35	$p < 0.01$
Sensitive bacteria	11	3	
Resistant bacteria	4	16	$p < 0.025$
Active PVE	3	20	
Healed PVE	13	17	$p < 0.05$
Infection localised to prostheses	8	13	
Extension of infection to myocardium or wall of great vessels	3	20	$p < 0.05$
PVE with CNS complications	4	11	
PVE without CNS complications	12	26	NS
Early PVE	0	11	
Late PVE	16	26	$p < 0.01$
Medical treatment	5	17	
Combined medical surgical treatment	11	20	$p < 0.05$

CNS, central nervous system; PVE, prosthetic valve endocarditis.

PROGNOSIS

We compared the 16 survivors with the 37 patients who died (table 8) to determine what factors were important to outcome. Five patients were lost to follow up (three survivors with combined medical and surgical treatment and two survivors with medical treatment). Congestive heart failure occurred in 94% (35/37) of those who died and in 50% (8/16) of survivors ($p < 0.01$).

Seventy eight per cent (11/14) of patients with bacteria sensitive to antibiotics survived and 21% (3/14) died; whereas 20% (4/20) of patients with resistant bacteria survived and 80% (16/20) died ($p < 0.025$).

Outcome was better when infection was restricted to the prostheses (13/21) or 61% mortality compared with 86% (20/23) mortality in extensive lesions.

Mortality from early prosthetic valve endocarditis was much higher (11/11) than that in patients with late prosthetic valve endocarditis (61% (26/42)).

A combination of medical and surgical treatment was associated with a slight improvement in outcome: 35% (11/31) vs 22% (5/22) in the medically treated group ($p < 0.05$).

Mortality in patients with neurological complications (74%) was not different from that in patients without such complications (72%).

Discussion

Prosthetic valve endocarditis is a serious and increasingly common complication of heart valve replacement; it is reported in 1–9, 4% of patients with prosthetic valve replacement.^{1–5} The high overall frequency (5.9%) in our series may be the result of inadequate prophylaxis. Clinical diagnosis is established by fever, leucocytosis, haematuria, cutaneous signs, splenomegaly, and the discovery at auscultation of new regurgitant murmurs.^{4,6} In 60% of our patients blood cultures were positive. The rate of negative blood cultures was high because many of our patients were referred from other hospitals and were already on antibiotics. Immunological abnormalities are a useful diagnostic feature in patients with negative blood cultures.^{7–9}

Like other workers,^{6,10–13} we too found that streptococci were the most common causal micro-organisms—followed by staphylococci, Gram negative bacteria, and fungi. Streptococci commonly cause late prosthetic valve endocarditis, often after treatment, whereas staphylococci, Gram negative bacteria, and *Candida* species are more important in early prosthetic valve endocarditis.^{3,6,14} The organisms are mainly acquired in the operating rooms or in the intensive care unit.³

There are differences in pathological findings between mechanical valves and bioprosthetic valves. In mechanical valves endocarditis is often associated with an infection behind the site of attachment of the prosthesis, resulting in ring abscess and dehiscence of the prosthesis.¹⁵ Extension of infection to adjacent cardiac structures is very common and it may cause a myocardial abscess, disruption of the atrioventricular conduction system, or fistulas into the right heart or pericardium.¹⁵ Vegetations are also common and they can be extensive, particularly in fungal infection. Ferrans *et al* found that bioprosthetic infection is usually localised to the cusps.¹⁶

Renal failure and nephrotic syndrome are rare,¹⁷ and due to a focal or diffuse glomerulonephritis and associated with immune complex in the serum and immunoglobulin deposits on the capillary wall.¹⁸

Mortality from prosthetic valve endocarditis is high, ranging from 35% to 71%.^{1,3–5,11–13} A new or an increased regurgitant murmur and the presence of congestive heart failure^{4,6} are associated with a very high mortality. We found 95% mortality in patients with heart failure compared with 50% in patients without congestive heart failure. The type of micro-organism is a major factor; patients with prosthetic valve endocarditis caused by less pathogenic organisms that are susceptible to antibiotic treatment respond better than those with prosthetic valve endocarditis caused by more invasive, anti-

biotic resistant bacteria.^{4,6,11} In the present series the mortality rate in streptococcal prosthetic valve endocarditis was 21% compared with 80% in non-streptococcal prosthetic valve endocarditis.

Extension of infection into the valve seat and adjacent tissues may result in partial or complete valve dehiscence, myocardial abscess, disruption of the atrioventricular conduction system, or fistulas into the right heart or pericardium. Our results and those of others^{6,19,20} suggest that invasion of the myocardium is associated with an increased mortality.

Mortality also varies with the time of onset of prosthetic valve endocarditis; most reports emphasise that prognosis is better in late prosthetic valve endocarditis^{6,10,12,13} than in early infection.^{11,20,21} This difference may be attributed to the predominance of streptococcal infection in late prosthetic valve endocarditis and the more pathogenic organisms seen in early prosthetic valve endocarditis, to immediate recovery from the operation, and to altered host resistance produced by the pump oxygenator.^{22,23} Neurological complications are an important cause of mortality and morbidity.⁶ Twenty five of the 33 deaths reported by Masur and Johnson were attributed to cardiac causes and eight to central nervous system events.⁴

Operation has dramatically improved the prognosis of prosthetic valve endocarditis. Gardner *et al* combined the results of treatment for prosthetic valve endocarditis of three published series and demonstrated a higher survival rate with combined valve replacement and antibiotic treatment compared with medical treatment alone.²⁴ Stinson *et al* successfully treated 12 of 17 patients with active prosthetic valve endocarditis by combined valve replacement and antimicrobial treatment; operative mortality was 24%.²⁵ These investigators recommend intervention irrespective of the stage of endocarditis.

Medical treatment alone should be used only in cases of prosthetic valve endocarditis caused by antibiotic sensitive micro-organisms, with unimportant or no prosthetic dysfunction, and when congestive heart failure and embolic events are absent.²⁶ Early operation combined with antibiotic treatment should be considered in all other cases.^{6,25} The main indications for operation are listed below: (a) Congestive heart failure with coexistent prosthetic dysfunction that does not respond to medical treatment.^{13,27} (b) Persistent sepsis after 7–10 days of appropriate antibiotic treatment or relapse after appropriate treatment or when fungal endocarditis is diagnosed. (c) Occurrence of an arterial embolus when echocardiography demonstrates residual vegetations¹³ or in the absence of abnormal echocardiographic findings when more than one arterial

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embolus occurs, or the presence of a single embolus which if exacerbated by a further embolic insult might result in irreversible neurological damage.^{6 12 19} (d) Conduction system abnormalities almost always indicate an annular abscess with extension to the septum¹³ and such lesions do not respond to medical treatment.^{19 28} (e) The appearance of new murmurs caused by fistulas into the right heart or pericardium or by septal rupture.²⁶

Conclusion

The high mortality in prosthetic valve endocarditis is mainly the result of congestive heart failure which is usually caused by prosthetic valve dysfunction. Mortality in early and late prosthetic valve endocarditis is reduced by prompt surgical intervention and adequate antibiotic treatment.

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