Prosthetic Valve Endocarditis - A Review

MUHAMMAD ABDUL AZIM
M B Y BILAL

Introduction:

Prosthetic valve endocarditis is one of the most serious and life threatening complication following cardiac surgery, equally dreaded by the patient and the surgeon. Improvements in cardiovascular diagnostics, better and increasingly adventurous cardiac surgery and greater access of cardiac surgery to patients are resulting in an ever-increasing number of survivors of successful cardiac surgical procedures. And so are health care professionals likely to encounter patients with this problem in their clinical practice.

Prosthetic valve endocarditis differs from native valve endocarditis in many ways, i.e., and the natural history, and the clinical manifestations, complications, mortality and management strategies. Because of relatively small number patients in most of the published studies, firm guidelines have not been developed for prevention, diagnosis and management of this special sub group of the patients. The publications on the topic, for the same reasons are relatively few. However, in face of high mortality, often exceeding 50%, it is important for cardiologists as well as primary care physicians to be conversant with essentials of management of prosthetic valve endocarditis. This article is an attempt to summarize current understanding of the subject with special emphasis on management strategies in our clinical environments.

Incidence:

Prosthetic valves are more prone to develop endocarditis as compared to even severely damaged native valves when controlled for all other risk factors. Infections of prosthetic valve account for 5-15% of all cases of infective endocarditis[1]. The overall incidence of endocarditis in prosthetic valve patients is 1-4%[2], or 0.5% per patient years[3]. The risk of developing prosthetic valve endocarditis is greatest at 15 days post-op (45 per 100000 patient days), rapidly declines thereafter, and from 150 days to 20 years remains stable at 1 episode per 100000 patient days.

Onset:

By convention, prosthetic valve endocarditis is termed early if it occurs within 60 days after surgery and late if it occurs later than that. This arbitrary separation, however, is much more than mere semantic. The etiology, microbiology and natural course of these two are substantially different. The incidence of prosthetic valve endocarditis in these two groups was nearly equally distributed, i.e., 1-2% at present, a reduction in early onset prosthetic valve endocarditis due to routine prophylactic antibiotic use.

The early onset prosthetic valve endocarditis is usually due to peri-operative contamination of prosthetic valves by direct inoculation, by-pass machine, vascular access lines, catheters, endotracheal tubes or pacing wires. The incidence of early prosthetic valve endocarditis has been greatly reduced, from 2.5% to 0.75% with routine use of peri-operative antibiotics.

Late onset prosthetic valve endocarditis, which occurs after endothelialization of prosthetic valves, usually involves the same mechanisms as that of native valves except that the causative organisms are those adapted to non-biological materials. As would be expected, the cumulative incidence increases with the duration of follow up.

Site:

The site most commonly involved in prosthetic valve endocarditis is aortic valve in sharp contrast to native valve endocarditis in which mitral valve involvement predominates. In one series, aortic valve prosthesis was involved in 63% of cases, mitral in 19% and double valves in 16%[2]. However, Slaughter et. al. reported an equal incidence of 3.8% in mitral and aortic

TABLE-1

Causative Organisms in Prosthetic Valve Endocarditis

Organism	Early PVE (%)	Late PVE (%)
Staph epidermidis	33	26
Staph aureus	17	12
Streptococci	7	30
Gram Negative Bacteria	19	12
Entercocci	2	6
Diphtheroids	10	4
Candida albicans	8	3
Aspergillus	1	0

prosthesis when controlled for number of valves implanted[4]. The reason for greater infection rate of aortic prosthesis has been postulated to be longer operation and by-pass timings and more turbulent flow. The incidence of prosthetic valve endocarditis in right-sided valves is exceedingly rare except in IV drug users. There is no definite pattern of involvement when two prosthetic valves are present. The infection rate of prosthetic valve implanted in patients with native valve endocarditis has been variably reported to be ranging form no increase to considerably higher, i.e. 5 times (4%)[5], but the infecting organism is usually different.

Valve Type:

There appears to be no significant difference in the cumulative risk of infection among mechanical and tissue prostheses. Valve make and model also does not seem to influence the rate. The time course of infection may, however, be different. It has been reported that mechanical prosthesis has a higher risk of infection during first three months of infection, but porcine valves had a higher risk at 12 months and later[6]. The mode of infection, however, is very different.

Risk Factors:

In one study, the most significant preoperative predictor of prosthetic valve endocarditis was active endocarditis at the time of operation. Early prosthetic valve endocarditis occurred more frequently in patients who underwent operation for multivalvular disease. Significantly related peri-operative variables were coma, prolonged mechanical ventilation, deep postoperative wound infection, postoperative jaundice, ventricular tachycardia, ventricular fibrillation, and replacement of more than one valve. Multivariate predictors were hypoxia, preoperative endocarditis, preoperative valve lesion, and resident surgeon. Significant preoperative variables predictive of late prosthetic valve endocarditis were mitral stenosis and mixed mitral stenosis-regurgitation. The only multivariate predictor of late prosthetic valve endocarditis was superficial wound infection[7]. Similar factors have been reported in other studies as well.

Microbiology:

The incidence of various organisms causing prosthetic valve endocarditis significantly differs among early and late onset endocarditis. In general, staphylococci dominate early onset type while streptococci are common in late onset type. Comparative frequency of causative organisms is given in Table-1. The list of causative organisms is growing incessantly and in future, due perhaps to wide spread antibiotic usage; the proportion of unusual organisms may assume significant proportions. It is of note that staphylococci still cause majority of early onset prosthetic valve endocarditis in spite of routine peri-operative use of staphylococcal antibiotics. Fungi, as gram negative bacteria cause prosthetic valve endocarditis with greater frequency as compared to native valves. These are thought to have been implanted at the time of surgery but may, at times, present as late onset endocarditis.

Factors contributing to development of early prosthetic valve endocarditis may be frequent intra-operative bacteremia (70%), faulty vascular access techniques, improperly designed operation room ventilation system, infected transfusions, presence of foreign body (prosthesis), infected operating room equipment, too much traffic in operating room and depressed immune system of the patient[8].

Pathology:

The hallmarks of prosthetic valve endocarditis are abscesses, progressive annular destruction, valve

dehiscence and destruction, para-valvular leaks, stenosis and extension of infective process to surrounding cardiac structures. Valve ring abscesses occur frequently and may be the major reason why medical treatment frequently fails.

The pattern of pathologic involvement in mechanical valves considerably differs from tissue valves. Infection of bioprosthesis primarily involves valve leaflets and sewing ring. Vegetations similar to native valve endocarditis form when leaflets are involved. Abscesses form early in the course of disease along the suture line and lead to para-valvular leaks, valve dehiscence or regurgitation. The incidence of valve ring abscesses, however, is considerably lower (16%) than mechanical valves. This lower incidence may be responsible for reported greater success with antibiotic treatment, i.e., 9% mortality in tissue valves treated with antibiotics as compared with 38% mortality in mechanical valves similarly treated[9].

In contrast, infection of mechanical valve almost always centres on the sewing ring and valve ring abscesses occur in 63% of cases. Progressive destruction of surrounding tissues occurs as with bioprosthetic valves. Vegetations are encountered rather infrequently. Inward growth of infective mass causes the occluder to become stuck in partially open or closed position.

Clinical Manifestations:

Prosthetic valve endocarditis differs from native valve endocarditis in its clinical manifestations in two important aspects: prosthetic valve infection may be extensive without usual clinical signs and valve dysfunction, when it does occur, tends to progress rapidly.

Fever is the most common presentation occurring in 97% of all cases. New murmurs are heard in just about half of the cases. Systolic murmurs are heard commonly in patients with prosthetic valves, but diastolic murmurs are distinctly absent: the presence, therefore, of a significant diastolic murmur should alert the clinician to the possibility of underlying endocarditis. Petechiae, Roth spots, Osler nodes and Janeway lesions are often absent. Splenomegaly is present in about one third of the cases. Congestive heart failure may be the presenting problem in many cases. Peripheral embolization occurs in 33% of cases with greatest frequency of nervous system involvement. Embolization is especially common in fungus endocarditis. Rarely, a septic shock like picture may be encountered. Haematuria and leukocytosis occur in about 50% of the cases[10]. Some cases of late onset bioprosthetic endocarditis may be very difficult to detect and an autoimmune disease like picture may be seen.

Diagnosis:

Blood Culture: The cornerstone of diagnosis of prosthetic valve endocarditis is positive blood culture. In contrast to native valve endocarditis, the bacteremia is continuous in prosthetic valve endocarditis. Blood cultures are positive in more than 99% of cases as compared with 75-95% in native valve endocarditis. Culture negative endocarditis is usually due to fungi, rickettsiae, diphtheroids, haemophillus and serratia species[7]. In one series, 75% of culture-negative endocarditis subsequently grew staph epidermididis[9]. Cultures have to be kept for three weeks to allow growth of fungi and other atypical organisms. Because of continuous bacteremia, it is unusual for cultures to be intermittently positive. In a study, first culture was positive in 95% cases while second was positive in 98% of the cases. There is no advantage to obtaining cultures from any specific site, time of day or body temperature, nor are arterial samples any superior[9]. At least 25% of blood cultures are negative if patient has used antibiotics in preceding 2-3 days. The diagnosis of endocarditis is generally accepted if 2 cultures are positive for the same organism in any patient with a compatible clinical syndrome of fever, splenomegaly or peripheral emboli when no other potential extra-cardiac source of bacteremia is discernable.

Differentiation of bacteremia of non-cardiac origin may be particularly difficult. Sande and co-workers found that bacteremia associated with following was unlikely to be associated with prosthetic valve endocarditis: (1) early post operative course (<25 days), (2) identifiable extracardiac source, (3) no murmur and (4) gram-negative organisms. On the other hand, bacteremia (1) that occurred after 25 days, (2) was caused by gram-positive organisms and (3) was associated with new and changing murmurs was more likely to be associated with endocarditis[11].

Echocardiography: Echocardiography is an excellent tool for diagnosis in native valve endocarditis with sensitivity and specificity above 90%. Unfortunately, this valuable non-invasive test is limited by false negative results due to acoustic shadowing caused by prosthetic valves, thus making identification of vegetations and abscesses difficult. The role of echocardiography involves (1) finding evidence for vegetations, (2) characterizing valvular dysfunction, (3) identifying periprosthetic spread of infection, and (4) determining preoperative prognostic data that impact on the need and timing of surgical intervention. Incorporation of echocardiography into the diagnostic criteria for endocarditis prevents delay in management and costly errors, particularly in patients with culture-negative infections and complications of the infection including jet lesions and deep tissue infections of the heart. TEE is particularly helpful in prosthetic valve endocarditis, because shielding by the prosthesis may prevent adequate transthoracic imaging, which give false-negative results[12]. In a study, prosthetic valve endocarditis and thrombi were correctly identified by TTE (transthoracic echocardiography) in 36% and 13% prostheses, respectively, but could be diagnosed by TEE in 82% and 100%, respectively. Compared with TTE, TEE had a higher sensitivity for morphologic prosthetic valve abnormalities in patients with either bioprostheses (87% vs 65%), or mechanical devices [83% vs 22%], and in patients with a prosthesis in either the aortic (77% vs 50%) or mitral (97% vs 65%) position. Overall, sensitivity and specificity were 57 and 63%, respectively, for TTE, and 86 and 88%, respectively, for TEE[13]. Colour doppler evaluation of prosthetic valves is an exciting prospect but more work requires to be done before any firm conclusions can be drawn. Echocardiography, moreover, can provide a lot of useful information regarding haemodynamic complications of prosthetic valve endocarditis. A word of caution: the detection of significant valvular regurgitation in patients with infective endocarditis who have not yet developed heart failure is not predictive of future complications nor does the absence of significant valvular regurgitation identify a group of patients with a more favourable prognosis. Therefore, decisions regarding clinical management in patients with infective endocarditis should not be made solely on the presence or absence of echocardiographically detected valvular regurgitation[14].

Isotope Studies: A few reports of diagnosing prosthetic valve endocarditis by radioisotope labeled leukocytes have been published. One report[15] using SPECT and Tc^{99} labeled anti-leukocyte antibodies gave results comparable to transesophageal echocardiography. Of note was the fact that it was able to detect presence of infection when TEE result was false negative. Though promising, the technique has little practical utility because of slow processing, high cost and limited availability.

Management:

There have been major changes in management strategies in prosthetic valve endocarditis over last couple of decades. Emphasis has shifted from medical management alone to early surgery, combined with antibiotics. Today, once the diagnosis of prosthetic valve endocarditis has been established, the decision making is rather straightforward. High morbidity and mortality associated with prosthetic valve endocarditis (overall 50%, fungal 90% and streptococcal 30%) and its rapid progression make immediate decisions mandatory. Once infected, almost all mechanical prostheses and more than 85% of bioprostheses require surgical replacement. Improvements in surgery have reduced the mortality of surgically treated prosthetic valve endocarditis to around 50% of that associated with medical management.

There, possibly, is a case for attempting medical treatment of a late onset endocarditis in a bioprosthesis when infection is due to low-risk organisms like streptococci and limited to valve leaflet or sewing ring only. However, if the infection is due to staphylococci, there develop new paravalvular leaks, sewing ring abscesses, valve dehiscence, major embolic phenomena or positive cultures persist more than one week after appropriate antibiotics, immediate resort to surgery should be made[16]. Guidelines for antibiotic treatment are generally similar to those for native valve endocarditis. Pending availability of culture sensitivity results, because of greater preponderance of staphylococci, empirical therapy with vancomycin, gentamicin and rifampicin should be started, to be later modified according to lab results.

Fungal endocarditis, being increasingly encountered, presents special difficulties in management. Extensive debridment combined with

valve replacement and prolonged systemic or oral anti-fungal drugs is the only approach, though recurrences are still common. Prolonged suppressive therapy with oral anti-fungal drugs has been shown to keep the patient in asymptomatic state[17,18].

Early surgery is of essence: there is little point in delaying surgery in hope of improving patients condition or achieving better results with longer pre-operative antibiotics. Although it has been observed that patients who received preoperative antibiotics for more than a week fared better than those who were given antibiotics for less than a week, but this has to be interpreted cautiously as the former group may be having better haemodynamic status and less extensive disease. Such a course of action has clearly shown to increase serious complications like refractory heart failure, renal failure or major emboli[19,20]. Like a bad tooth, an infected prosthesis is better out than inside, and the sooner the better. A reasonable compromise would be that if there is no evidence of heart failure, patients might be given antibiotics for a week. Meanwhile, close observation and serial TEE should be done to detect any signs of hemodynamic deterioration. Once the evidence of heart failure is observed, the patients should be taken to surgery at the earliest possible.

The surgical treatment, in essence, involves debridment of infected material, replacement of infected valve and reparative procedures as dictated by nature and extent of damage. A host of re-constructive procedures are being reported employing various prosthetic materials. The detail of these is beyond the scope of this article.

Guidelines for prevention of endocarditis in prosthetic valve recipients are similar to those recommended for high-risk group by Committee on Rheumatic Fever and Infective Endocarditis of the Council on Cardiovascular Disease in the Young of American Heart Association[21]. The patients should be fully explained about the preventive measures and detailed written follow up provided.

Conclusion:

Prosthetic valve endocarditis is the dreaded complication of cardiac surgery. Subtle symptoms, atypical signs and presentation, diagnostic difficulties coupled with high mortality necessitates earliest possible diagnosis and prompt management decisions. A high index of suspicion on part of primary care physicians and prompt referral to a cardiac center can not be over-emphasized. Once diagnosed, earliest possible surgical intervention should be aimed at.

For Correspondence:

Col. M.B.Y. Bilal, FCPS, Armed Forces Institute of Cardiology, Rawalpindi.

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