What do We Know about Early Prosthetic Valve Endocarditis?

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1. Definition and Epidemiology

Definition:

The classification of early or late prosthetic valve endocarditis is determined by the time span between surgery and the appearance of symptoms and signs of the disease. However, it is not always easy to establish the exact moment of the beginning of the clinical manifestations; especially, in chronic and sub-acute endocarditis. It is important to understand the concept of early prosthetic endocarditis; it is an infection acquired in the perioperative period, and therefore, it has a particular epidemiology, microbiology, clinical manifestations and treatment. On the other side, there is no agreement about the cut point for this classification. In some studies early prosthetic endocarditis is diagnosed when the disease occurred in the first two months after surgery [1-4], while in other studies this period is six [5-7] or twelve months [8-9].

In a recent report, there were not significant differences in the microbiological profile when endocarditis developed in the first two months after surgery or between the two months and the first year after surgery [9]. Nevertheless, the proportion of cases due to coagulase-negative staphylococci was significantly higher (37 versus. 18%, p= 0.005) in the first year after the intervention whereas estreptococcus viridans was more frequent in prosthetic valve endocarditis that appeared after the first year of surgery (18 versus. 1%, p= 0.001). With these results we think that the cut point to speak about early prosthetic valve endocarditis should be twelve months after surgery.

Epidemiology:

The incidence of early prosthetic valve endocarditis has decreased in the last years, thanks to better measures of prevention in perioperative infections (including antibiotic prophylaxis in valvular surgery), and also probably, to the generalization of prophylaxis in all procedures that entail bacteraemia in patients with a prosthetic valve. However, the absolute number of cases is increasing because the number of valvular replacements has been multiplied in the recent years. Nowadays, prosthetic valve endocarditis represents approximately 10-30% of all cases of endocarditis in the developed countries [3]. The risk to develop an infective endocarditis after valvular replacement depends on the time from surgery. The risk is greater in the first six months (mainly between the 15 and 45 first days), although it remains increased until the first year (1-3%), and becomes stable later [1,2,5,10,11]. Therefore, early prosthetic valve endocarditis has higher incidence than late prosthetic endocarditis.

The risk factors to develop an early prosthetic valve endocarditis are advanced age, preoperative endocarditis, prolonged time of surgery, and multivalvular replacement. Some authors suggest that early prosthetic valve endocarditis is more frequent in the aortic position [12] and that the mechanical prosthesis get infected more frequently in the first months while the biological ones become infected later [10].

2. Pathogenesis and Microbiology
Pathogenesis

Early prosthetic endocarditis is defined as that infection that is acquired during the perioperative period. The main factors that favour the adhesion of the microorganisms are the lack of endothelization of the prosthetic ring and the injured perivalvular tissue along suture pathways (mainly valvular ring). The infection can be originated by direct intraoperative contamination or by hematogenic dissemination secondary to nosocomial infections in the first weeks after surgery. During the surgical procedure, the extracorporeal circulation pump and the suction pump have been pointed as reservoirs of microorganisms [13]. This is why, the risk of early prosthetic endocarditis is increased when the time of extracorporeal circulation is high.

Respecting nosocomial infections that can produce bacteraemias, the most frequent are the infection of the surgical wound and intravascular catheters that have been used for post-surgical haemodynamic control [11,13,14]. On the other hand, the presence of previous endocarditis (reason for the valvular replacement) is a risk factor for the development of prosthetic endocarditis and if this endocarditis appears early after surgery, we have to think that it can be a relapse.

Microbiology:

The most frequently encountered pathogens in early prosthetic endocarditis are coagulase-negative staphylococci (32-56%), and almost all of them are S. epidermidis. The second microorganism in frequency is S. aureus, which represents 15-24% of the cases, approximately [9,13,15]. Unto 77% of these microorganisms are methicillin-resistant [9].

Nevertheless, the microbiology of prosthetic endocarditis is might be changing. In a recent article that takes as a cut point for early prosthetic endocarditis, the first two months, the most frequent microorganism isolated was S. aureus (35.9%), followed by coagulase negative staphylococcus (17%) [3].

Others pathogens that can cause early prosthetic endocarditis are fungi (4-12%), enterococcus (7,5 - 11%), gram-negative bacilli (5-13%), streptococci (1-2%) and difteroides (4-7%). Blood cultures are negative in 5-17% of the cases, probably related to the prompt initiation of antimicrobial therapy.

Table 1 and 2 summarize the microbiological profile of early prosthetic endocarditis according to the cut point (two or twelve first months after surgery).

<table>
<thead>
<tr>
<th>MICROORGANISM</th>
<th>EARLY PROSTHETIC ENDOCARDITIS &lt; 2 MONTHS</th>
<th>LATE PROSTHETIC ENDOCARDITIS &gt; 2 MONTHS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Coagulase-negative staphylococci</td>
<td>121 (30%)</td>
<td>229 (24%)</td>
</tr>
<tr>
<td>Staphylococcus aureus</td>
<td>77 (19%)</td>
<td>151 (16%)</td>
</tr>
<tr>
<td>Streptococci and enterococci</td>
<td>40 (10%)</td>
<td>337 (35%)</td>
</tr>
<tr>
<td>Gram-negative bacilli</td>
<td>63 (16%)</td>
<td>59 (7%)</td>
</tr>
<tr>
<td>Anaerobes</td>
<td>24 (6%)</td>
<td>11 (1%)</td>
</tr>
<tr>
<td>Fungi</td>
<td>46 (11%)</td>
<td>38 (4%)</td>
</tr>
<tr>
<td>Others</td>
<td>6 (2%)</td>
<td>21 (2%)</td>
</tr>
<tr>
<td>Negative cultures</td>
<td>24 (6%)</td>
<td>89 (9%)</td>
</tr>
<tr>
<td>Total</td>
<td>401</td>
<td>945</td>
</tr>
</tbody>
</table>

Table 1. Microbiological profile when early prosthetic valve endocarditis is defined within the first two months [3,13].
3. Pathology

The main lesion of the prosthetic valve endocarditis is the same as in native valve endocarditis: the vegetation. Nevertheless, there are a few histological characteristics in early-onset prosthetic valve endocarditis: mainly, periannular complications are more frequent (abscesses, pseudoaneurysms and fistulas). This is probably due to the pathogenesis of the disease. The material implanted is not yet endotheliized, and the nosocomial microorganisms are more virulent, so the infection is more "aggressive" and locally invasive. In addition, the endothelium of perivalvular tissue along suture pathways is injured, and the synthetic material of mechanical prosthetic valves makes difficult to the microorganisms to grow over it [13]. Periannular complications are more frequent in prosthetic aortic valves, and they can be present in almost 53% of the cases [6,7]. Perivalvular invasion can cause a dehiscence of the prosthesis and different degrees of paravalvular regurgitant flow. Moreover, in the case of aortic endocarditis, the infection can disrupt the conduction system and reach the mitroaortic continuity or the anterior leaflet of the mitral valve (Fig. 1). In bioprosthetic valve endocarditis, it is more common to find vegetations in the valve and sometimes perforation of the leaflets resulting in valvular dysfunction and regurgitation (Fig. 2).

<table>
<thead>
<tr>
<th>MICROORGANISM</th>
<th>EARLY PROSTHETIC ENDOCARDITIS &lt; 12 MONTHS</th>
<th>LATE PROSTHETIC ENDOCARDITIS &gt; 12 MONTHS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Coagulase-negative staphylococci</td>
<td>109 (50%)</td>
<td>14 (14%)</td>
</tr>
<tr>
<td>Staphylococcus aureus</td>
<td>31 (14%)</td>
<td>17 (16%)</td>
</tr>
<tr>
<td>Streptococci and enterococci</td>
<td>20 (9%)</td>
<td>46 (46%)</td>
</tr>
<tr>
<td>Gram-negative bacilli</td>
<td>12 (5%)</td>
<td>12 (12%)</td>
</tr>
<tr>
<td>Anaerobes</td>
<td>8 (4%)</td>
<td>1 (1%)</td>
</tr>
<tr>
<td>Fungi</td>
<td>18 (8%)</td>
<td>2 (2%)</td>
</tr>
<tr>
<td>Others</td>
<td>3 (1%)</td>
<td>3 (3%)</td>
</tr>
<tr>
<td>Negative cultures</td>
<td>19 (9%)</td>
<td>6 (6%)</td>
</tr>
<tr>
<td>Total</td>
<td>220</td>
<td>102</td>
</tr>
</tbody>
</table>

Table 2. Microbiological profile when early prosthetic valve endocarditis is defined within the first twelve months [9,13].

Figure 1: Abscess in the the mitroaortic continuity (*)
The clinical manifestations of patients with prosthetic valve endocarditis are similar to those encountered in native valve endocarditis. Moreover, there are not very important differences between early and late prosthetic valve endocarditis. Nevertheless, there are a few clinical characteristics that should be mentioned. First of all, as we have already mentioned in pathogenesis and pathology sections, it is quite frequent to find periannular complications and adjacent tissue invasion that can cause conduction disturbances with different degrees of auriculo-ventricular block. Moreover, if there is valvular dysfunction with stenosis or regurgitation due to vegetations on the prosthetic valve, we can find new murmurs, and signs and symptoms of congestive heart failure. On the other hand, the early infection can be hidden by symptoms related to the surgery and/or other perioperative complications, including urinary tract infections, phlebitis, respiratory tract infections or infection of the surgical wound [13].

About the diagnosis of prosthetic valve endocarditis, it should be the same as for the native valve endocarditis, and it should be done with the modified Duke University criteria [16]. In the postoperative period of cardiac surgery, the blood cultures positive predictive value to diagnose endocarditis is lower than in other clinical contexts, because they can reflect an extracardiac bacteremia. This happen generally with positive blood cultures for gram-negative bacilli and in the first month after surgery, so in these cases we always have to exclude an extracardiac origin of the infection. [13,17].

Echocardiography is a very important technique for the diagnosis and management of infective endocarditis. In the case of the prosthetic valve endocarditis, we generally need to perform a transesophageal echocardiography. Its sensibility to detect periannular complications is higher thus that of transthoracic echocardiography, reaching 90-100% in some studies. [6] (Fig. 3.)
5. Treatment

Anticoagulant Therapy:

If anticoagulation is necessary, it should not be discontinued; in these cases, intravenous heparin is recommended because the anticoagulant effect can be interrupted quickly if it is necessary [4]. If the patient suffers a stroke, anticoagulation should be temporarily discontinued, in order to avoid the hemorrhagic transformation of the stroke, moreover, there are no studies that give evidence that anticoagulation prevents new emboli in these cases [18]. Anyway, the final decision about anticoagulation therapy should be taken individually, considering its risks and benefits.

Antimicrobial Therapy:

The general principles for antimicrobial therapy are the same as for native valve endocarditis. The recommendations include the intravenous administration of the antibiotics, during six to eight weeks, based on the antibiogram, and including at least one bactericidal agent [4,8,13]. Empiric antibiotic therapy can be initiated after obtaining blood cultures if the patient presents with hemodynamic instability or fatal clinical course. If early-onset prosthetic valve endocarditis occurs in the first year after valve replacement, the antimicrobial treatment chosen must be active against the more frequent microorganisms envolved, which are, as we mentioned before, methicillin-resistant Staphylococcus. In these cases, the therapy recommended is the combination of vancomycin (15 mg/kg i.v / 12 h) plus rifampin (300 mg p.o. / 8 h) during at least six weeks, and adding gentamicin (1 mg/kg i.v. / 8 h) during the two first weeks of the treatment [4,8,19].

Surgery:

No randomized controlled studies have evaluated the optimal indications for surgery in the early-onset prosthetic valve endocarditis. Some authors suggest that surgery should always be indicated if the prosthetic valve endocarditis presents in the first two [20] or twelve [8] months. Nevertheless, the recent 2006 American College of Cardiology/American Heart Association (ACC/AHA) guidelines on the management of valvular heart disease [4] are only based upon clinical criteria, and not upon the time from the valve replacement (Table 3). In our opinion, the ethiology of the early-onset prosthetic valve endocarditis is essential to decide if surgery is indicated. If the endocarditis is caused by S. aureus, fungi, pseudomones or other virulent microorganisms, we recommend urgent surgery.
Class I:
- Patients who present with heart failure (level of evidence: B).
- Prosthetic disk failure evidenced by cine fluoroscopy or echocardiography (level of evidence: B).
- Evidence of increasing obstruction or worsening of a previous valve regurgitation (level of evidence: C).
- Patients who present with complications (e.g., abscess formation) (level of evidence: C).

Class IIa:
- Evidence of persistent bacteremia or recurrent emboli despite appropriate antibiotic treatment (level of evidence: C).
- Relapsing infection (level of evidence: C).

Table 3. Recommendations for Surgery in Prosthetic Valve Endocarditis [4].


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