Surgical treatment of infective endocarditis with special reference to prosthetic valve endocarditis

S WESTABY, CELIA OAKLEY, R N SAPSFORD, H H BENTALL

Abstract

Patients with native valve endocarditis treated surgically between 1968 and 1978 (n = 15) and all patients presenting with prosthetic valve endocarditis during this period (n = 21) were followed up for at least four years. Five of the patients with native valve endocarditis required urgent early surgical intervention, of whom two died. The remaining 10 underwent valve replacement after a course of antibiotic treatment: all survived, though one required further valve replacement. The 21 patients with prosthetic valve endocarditis suffered 25 attacks. Nine were cured by medical treatment alone; two died before surgical intervention was possible; 11 required valve replacement, of whom three died; and two required valve replacement after a course of antibiotic treatment. The incidence of early prosthetic valve endocarditis—that occurring within two months of operation—was 0.67%, but that of late prosthetic valve endocarditis could not be determined.

Medical treatment when started early should cure endocarditis in most patients, but vigilance should be maintained for the appearance of indications for surgery. When such indications exist surgery should not be delayed.

Introduction

The introduction of effective chemotherapy and development of valve replacement surgery have dramatically changed the outlook for patients with infective endocarditis. Since Wallace et al. first reported successful excision and replacement of the valve in patients with active disease the role of surgery in the treatment of this condition has expanded steadily. Initial reluctance to insert a substitute prosthetic valve into an infected site diminished when emergency valve replacement proved life saving for patients with rapid haemodynamic deterioration, uncontrollable infection, or recurrent embolism, in whom the mortality with continued medical treatment approached 100%.1,2

Prosthetic valve endocarditis is a “new” disease that may occur early or late after valve replacement. Late infection develops as part of a continuing long term risk when bacteraemia from an infected organism occurs. The infecting organisms are similar to those found in patients with native valve endocarditis.3 When infection appears within two months of operation it is usually attributable to contamination at the time of valve replacement, particularly after sternal wound infection, and an incidence of 10% in the early 1960s has been reduced to 1% or less with the introduction of more effective antistaphylococcal prophylaxis.4

Perhaps more than any other condition the treatment of both primary and prosthetic valve endocarditis requires close cooperation between cardiologist, bacteriologist, and cardiac surgeon at an early stage of the disease. Surgical intervention, when required, must be carefully timed. Ten years ago Wise et al at this hospital advocated prompt replacement of the aortic valve for patients with severe acute aortic regurgitation despite active endocarditis.5 We describe the patients with infective endocarditis who have needed surgical treatment at this hospital since that time.

Patients and methods

The definition of infective endocarditis for the purpose of this study was an illness producing valvular dysfunction and incorporating characteristic clinical features that include fever, new cardiac murmurs, splenomegaly, or embolic manifestations. Positive blood cultures were obtained in 77% of attacks. Some patients at presentation had already received blind antibiotic treatment, and a few, in whom the diagnosis was initially made serologically, had infections caused by cell dependent organisms (Coxella or Chlamydia). Demonstration of typical vegetations by echocardiography, at surgery, or at necropsy was held as confirmation of infective endocarditis.

Twenty seven patients were operated on for endocarditis between 1968 and 1978 and were followed up for at least four years, 15 with native valve (primary) endocarditis and 12 out of 21 patients who presented with prosthetic valve endocarditis. Patients whose native valve endocarditis was successfully treated medically or for whom valve replacement was required at some time remote from the infection were not included. All patients with prosthetic valve endocarditis were included, though not all required surgical treatment.
When infective endocarditis was diagnosed clinically antibiotic treatment was started immediately after blood samples were taken for culture and before laboratory information was received. In the case of primary endocarditis treatment usually consisted of a combination of benzylpenicillin and gentamicin both given intravenously in bolus dosage. After the organism responsible had been isolated by blood culture bacterial efficiency was tested and the drugs altered appropriately.

Throughout the course of medical treatment patients were watched carefully for evidence of clinical deterioration, including embolism. Echocardiography was increasingly used to detect vegetations as the two dimensional technique is of great value in assessing their size and mobility and so the risk of embolisation. Aortography was used when indicated to show local tissue destruction, including paravalvular abscess, though more recently two dimensional echocardiography has largely taken this role. In patients with rheumatic heart disease and valve surgery unhesitatingly undertaken in the active phase of the disease, particularly in cases of endocarditis caused by coagulase positive staphylococci.

Indications for surgical intervention were: (i) increasing valvular regurgitation before, during, or after antibiotic treatment; (ii) systemic embolism (particularly if each, cardiology showed persisting large or mobile vegetations; (iii) removal of an infected leaking valve prosthesis during or after a full course of antibiotic treatment; (iv) a paravalvular abscess recognised by aortography or two dimensional echocardiography, or both, and often suspected by new conduction defects and continuing bacteraemia; and (v) infection by antibiotic resistant organisms such as candida, or continuing evidence of infection despite apparently sensitive organisms.

After operation treatment was continued for as long as deemed necessary from the surgical findings, bacteriological studies, duration of preoperative treatment, and clinical state. For patients who had been operated on while in infection was still active the postoperative duration of treatment was usually six weeks.

**Results**

**Surgery for primary infective endocarditis**

Fifteen patients (nine men, six women) required valve replacement for primary infective endocarditis. Five patients gave a history of rheumatic fever, and in three there was a known congenital cardiac anomaly: in two this was a bicuspid aortic valve and in the third a ventricular septal defect. The remaining seven patients had no previous history of possible heart disease. Recent dental manipulation had been carried out without antibiotic prophylaxis in two patients. One had suffered meningitis with streptococcal infection and one was a narcotic addict. The remaining attacks were without a known source of infection.

The aortic valve was affected primarily in five attacks, the mitral valve in five, and the tricuspid valve in two. Both mitral and aortic valves were affected in three attacks. Of the eight patients with aortic valve infection, three had an aortic root abscess excavating the ventricular septum.

**Bacteriology**—The table shows the microorganisms responsible for infection. A variety of organisms were implicated, but most common were streptococci of the viridans group (this includes *Streptococcus mutans*, *Streptococcus mitis*, *Streptococcus milleri*, and *Streptococcus sanguis*). Negative cultures were obtained in three patients.

**Results of treatment**—Early haemodynamic deterioration due to valve destruction and aortic or mitral regurgitation required surgical intervention during the active stage in five patients including the patient with a ventricular septal defect and aortic valve infection. This patient underwent aortic valve replacement with closure of the ventricular septal defect and recovered uneventfully. All five patients had evidence of systemic embolism with persisting infection and vegetations on the valve. Thus, as in most patients operated on at this stage, the indications for surgery were multiple. One patient died on the operating table and another from ventricular fibrillation on the second postoperative day. Ten patients underwent valve replacement after a full course of treatment, four because of persisting infection and six with damaged and regurgitant valves. Three of the patients with persistent bacteraemia were found to have cavitation and an abscess in the aortic root. All patients in this group survived operation, though one man with an aortic root abscess developed a large para-prosthetic leak afterwards and required further valve replacement.

**Bacteriology** (table)—Staphylococci were most commonly implicated in both early and late prosthetic valve endocarditis, but the numbers were small. Most showed resistance to benzylpenicillin, and other antibiotics were used in their treatment but always in combination since many showed multiple resistance. *Staphylococcus aureus* occurred more frequently than *Staphylococcus epidermidis* in patients with late endocarditis. Streptococci were responsible for one third of cases of late endocarditis in which a positive culture was obtained but were implicated only

<table>
<thead>
<tr>
<th>Organism</th>
<th>Native valve endocarditis requiring valve replacement</th>
<th>Prosthetic valve endocarditis</th>
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<tbody>
<tr>
<td></td>
<td>Total</td>
<td>Early</td>
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<tr>
<td><em>Streptococci:</em></td>
<td></td>
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<tr>
<td><em>Staph viridans</em></td>
<td>6</td>
<td>3</td>
</tr>
<tr>
<td><em>Staph aureus</em></td>
<td></td>
<td></td>
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<tr>
<td><em>Staph epidermidis</em></td>
<td>1</td>
<td>2</td>
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<tr>
<td>Other*</td>
<td>5</td>
<td>3</td>
</tr>
<tr>
<td></td>
<td>Total</td>
<td>15</td>
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*Theatre contamination but late in presentation.

1 Usually either streptococcal or cell dependent organisms (Coxella or Chlamydia), 225 attacks in 21 patients.

**Prosthetic valve endocarditis**

Twenty one patients (11 men, 10 women; age range 21-68) suffered 25 attacks of endocarditis on a valve prosthesis. Ten attacks occurred within two months of valve replacement and were classified as early prosthetic valve endocarditis; 15 attacks occurred late. Two attacks of *Streptococcus viridans* infection, preceded two early attacks of *Staphylococcus epidermidis* infection, and one patient developed early *Staph aureus* infection on both mitral and aortic valve prostheses after insertion of a percutaneous transvenous pacing wire. Dental treatment preceded two late attacks of *Staph aureus* prosthetic valve endocarditis followed acute cholecystitis and instrumentation of a urethral stricture respectively. Two attacks of late prosthetic valve endocarditis with klebsiella occurred in patients who had undergone valve replacement in the same operating theatre on consecutive days, and though late in presentation this evidence points to contamination in the operating theatre.

Infection occurred on an aortic prosthesis in 10 cases and a mitral prosthesis in five. Simultaneous infection on both mitral and aortic prostheses occurred in four patients with double valve replacements and on both mitral and tricuspid prostheses in two other patients. In four of the 14 infected aortic prostheses an aortic root abscess excavated the ventricular septum. Both Starr-Edwards and Bjork-Shiley prostheses had been used, but there were no differences in the incidence of infection between the two. One man with a Dacron graft replacement of both ascending thoracic and abdominal aorta and a bicuspid aortic valve developed salmonella endocarditis with aortic regurgitation. This case the gall bladder probably harboured the infecting organism.

**Results of treatment**—Nine patients, all with late prosthetic valve endocarditis, were cured by antibiotic treatment alone and required no further surgery. Three patients died without further surgery, the first with an obstructed Bjork mitral prosthesis, the second with a burst myotic aneurysm around an infected Starr-Edwards aortic valve prosthesis, and the last after late presentation with a large paraprosthetic leak, severe cardiac failure, and septicaemia. Eleven patients (four with early and seven with late prosthetic valve endocarditis) required emergency replacement at an early stage for progressive valve disease and haemodynamic deterioration. Six of these patients recovered with the prosthesis intact. In two patients without severe haemodynamic deterioration bacteraemia persisted despite appropriate antibiotic treatment and aortography showed them to have an aortic root abscess with a small paraprosthetic leak. In both cases the leaking aortic prosthesis was replaced and the patients recovered uneventfully with continued chemotherapy. Two survivors developed a paraprosthetic leak around the new valve, one of whom required a further valve replacement soon afterwards. Three patients died after surgery, one after cerebral embolism, the second with bronchopneumonia, and the third with renal failure.
once in cases of early endocarditis. In five cases (three early, two late) negative cultures were obtained; the three patients with early endocarditis had received perioperative prophylaxis and the two with late endocarditis had been given blind antibiotic treatment.

Prosthetic valve endocarditis after valve replacement between 1968 and 1978—During the course of this study the prophylactic antibiotic regimen for patients undergoing cardiac surgery usually comprised penicillin, cloxacillin, and streptomycin given parenterally for five days beginning on the morning of operation. Altogether 1488 operations for valve replacement were carried out at this hospital during this period. Ten patients were known to have developed prosthetic valve endocarditis within two months of operation and three patients died. The incidence of early prosthetic valve endocarditis in this series was therefore 0·67%. The true incidence of late prosthetic valve endocarditis was difficult to establish and results unknown since several patients were treated without ever being readmitted to this hospital.

Discussion

Two major advances in treatment dramatically changed the prognosis of patients with infective endocarditis. The first was the introduction of effective chemotherapy and the second the recognition that surgical intervention during active endocarditis could save those patients who would otherwise die from the haemodynamic consequences of the disease.1–4 Indeed, the first successful surgical operation during active endocarditis was carried out by Tubbs, who ligated an infected ductus arteriosus and removed the infection before the days of penicillin. Infective endocarditis is curable, and the continuing overall mortality—estimated as up to 30%—may be wholly attributed to late diagnosis and poor management.

Previous reports have shown the efficacy of timely surgical intervention,10–12 but the need for surgery is itself a reflection on management and usually means that the onset of treatment had been delayed. Advanced destruction of a native valve or dehiscence of a prosthetic valve was the commonest reason for urgent surgical intervention, though most of our patients had multiple indications on referral. During this study eight other patients with native valve endocarditis were transferred when they were already moribund and died almost immediately after arrival before surgery could be contemplated. Sixteen patients, notably 11 with prosthetic valve endocarditis, required urgent valve replacement for valve failure that would otherwise have quickly led to a fatal outcome. Inevitably, operative morbidity and mortality in this group of patients is substantial.

Deterioration in valve function may be rapid at an early stage, particularly in Staph aureus infections and particularly also in the young with non-calcified, thin, bicuspid aortic valves. Antibiotics and surgery must never be delayed until the infection is no longer haemodynamically significant. Failure to treat at the earliest possible stage is lethal and the delay may be months in late endocarditis. In the presence of aortic regurgitation, surgery is not a high-risk procedure even when it is performed late.6

Why is infective endocarditis so much more resistant to treatment? The causes of antibiotic treatment failure in infective endocarditis are not clear. Many patients in whom infection is established have advanced lesions, and in others, typical infective endocarditis is only one aetiological factor in a complex clinical situation. Late endocarditis is most often caused by antibiotic-resistant organisms.16,45

Discussion

This section discusses the implications of the findings and the conclusions drawn from the study. It is important to note that the discussion should not repeat the findings or conclusions presented in the results, and that it should be focused on the broader implications of the research for the field of medicine. The discussion should provide a comprehensive overview of the findings, and should acknowledge any limitations or weaknesses of the study. It should also consider the implications of the findings for clinical practice, research, and policy-making. The discussion should be written in a clear and concise manner, and should provide evidence-based insights into the significance of the findings.

Conclusion

In conclusion, the findings of this study demonstrate the importance of early intervention and effective antibiotic treatment in the management of infective endocarditis. The results highlight the need for improved diagnostic tools and increased awareness of the disease. The study also suggests that further research is needed to identify the underlying causes of antibiotic treatment failure in this condition. The findings have significant implications for clinical practice, and should be considered in the development of guidelines for the management of infective endocarditis.
late prosthetic valve endocarditis were satisfactorily treated with antibiotics alone, and the success of medical treatment in this group might be as high as that in patients with native valve endocarditis despite the foreign body mass. Since infection occurs at the interface of the tissue annulus and rigid prosthesis, disruption of sutures in early prosthetic valve endocarditis may occur even with organisms of low virulence, but in late prosthetic valve endocarditis with tissue ingrowth a new leak means entrenched infection. These factors, with the added proviso that the patients may have only limited haemodynamic reserve from the pre-existing valvular heart disease, dictate that indications for operation should be more aggressive than those in primary endocarditis, which should be cured by early medical treatment before haemodynamic deterioration occurs.

Three of the most serious complications of prosthetic valve endocarditis—namely paraprosthesis leak with severe left ventricular failure, obstruction of a tilting disc prosthesis, and burst myotic aneurysm—were responsible for the deaths of those patients who died without further operation. As in other series12 17 18 a large proportion of patients with prosthetic valve endocarditis required operation during the active stage of the disease compared with patients with primary endocarditis. Early prosthetic valve endocarditis in particular has a high prevalence of staphylococcal infection, and the organisms may well be sensitive to the antibiotics used in prophylaxis. This possibility must not be ruled out when treatment is considered. Our experience caused us to change the prophylactic regimen, and antibiotics are no longer started early but the first dose is given intravenously by the anaesthetist immediately before the skin incision.

Fungal infection with Candida albicans accounted for one late case of prosthetic valve endocarditis in this series and may present early or pursu an indolent course with delayed recognition for a year or more.1 Primary aetiological factors for this type of endocarditis are prolonged antibiotic treatment, general debility, and the use of steroids.9 Late bacterial infections presumably arise after transient bacteraemia, particularly after procedures such as urinary tract manipulation or dental treatment. Awareness of the prosthetic valve should make adequate antibiotic prophylaxis much easier in this group, and endocarditis should be suspected early if there is unexplained fever or malaise. It is vital to remember that constitutional signs such as anaemia, weight loss, clubbing, or splenomegaly take weeks to develop, by which time medical cure may no longer be possible because of dehiscence of the prosthetic valve ring. An important contributory cause of late diagnosis has been expectation of a change in prosthetic valve sounds, a naive concept since no change in prosthetic valve function occurs until there is either dehiscence or interposition of a large vegetation between the moving parts, both of which are late events.

Conclusion—Cardiac surgery has been responsible for both a dramatic improvement in the outlook of patients with infective endocarditis and for a new disease—namely, prosthetic valve endocarditis. When indications exist for surgery after endocarditis, this must not be delayed because only by this means can haemodynamic correction be achieved, the bulk of the infected material removed, and embolism of persisting vegetations prevented. Medical treatment if started early should cure most patients but continuous vigilance should be maintained for the appearance of indications for surgery.

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References


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