Surgery for infective valve endocarditis in children

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Abstract

Objective: Surgery for endocarditis in children is relatively uncommon. Our aim is to assess operative mortality, recurrent infection, re-operation and long-term survival rates following surgery for infective valve endocarditis in children. Patients: Sixteen consecutive children (ten female, six male, mean age 11.8 years, range 25 days–16 years) undergoing surgery between 1972 and 1999 in Southampton were studied. The aortic valve was affected in five, mitral in four, aortic and mitral in one, tricuspid in five and a pulmonary homograft in one patient. Prosthetic valve endocarditis was present in three. Twelve surgical interventions were emergency and four urgent. Indications for operation included cardiac failure in five, severe valvular dysfunction in nine, vegetations in nine, persistent sepsis in four and embolization in four patients. The offending micro-organism was identified in 13. Valve replacement was performed in 11 and excision of vegetations in two and excision of vegetations and repair in three. Follow-up was complete (mean 11.2 years, range 2 months to 26.3 years, total 179.5 patient years).

Results: There was one operative death (6.2%) in a 25-day-old neonate who presented in a moribund condition. Endocarditis recurred in one patient (6.25%). Freedom from recurrent infection at 10 and 20 years was 100.0 and 87.5%. Seven surgical re-interventions were required in four (25.0%) patients with no operative mortality. Freedom from re-operation at 1, 5, 10 and 20 years, was 84.6, 76.1, 76.1 and 60.9%, respectively. Two patients died 15 and 23 years after their first operation. The cause of the late deaths was non-cardiac in the first and unknown in the other. Actuarial survival, including operative mortality, at 1, 15 and 20 years was 93.7, 93.7 and 78.1%. Conclusions: Surgery in children with infective valve endocarditis can be performed with low operative mortality. Although some patients may require re-operation, freedom from recurrent infection and long-term survival are satisfactory. © 1999 Elsevier Science B.V. All rights reserved.

Keywords: Surgery; Endocarditis; Children

1. Introduction

Infective endocarditis remains relatively uncommon in children, its incidence, however, according to several recent reports, appears to be increasing [1–3].

Although the ‘healthy’ paediatric population is not immune, children with untreated congenital heart disease (CHD), notably ventricular septal defect and patent ductus arteriosus, are considered to be at higher risk as are the children with complex intra-cardiac abnormalities undergoing surgical palliation or definitive correction [1–5].

Despite reports on improved outcomes over time [2], infective endocarditis in infancy and childhood remains a most serious condition. Hospital mortality rates of 10.0–20.0%, following medical treatment alone, are not unusual [1–3,5] whereas surgical intervention, frequently employed as a last resort in severely compromised patients, has been associated with variable peri-operative death rates ranging from 0 to 50.0% [3–10].

The purpose of this study, besides reviewing the clinical and pathological features, was to determine the incidence of operative death, recurrent infection, re-operation and long-term survival rates following surgical intervention for active infective valve endocarditis in infants and children.

2. Patients and methods

Between January 1973 and March 1999, 16 consecutive children underwent surgical treatment for infective endocarditis in Southampton. There were ten females and six males with a mean age of 11.8 years, range 25 days–16 years.

Criteria used for establishing the diagnosis of endocarditis in this study were those originally described by Saiman et al. [11] and modified by Martin et al. [1]: (1) Positive blood cultures for a pathogen in at least two separate cultures, or persistently over time, with a vegetation on echocardiography in a patient with or without structural heart disease.
At least two positive blood cultures for *Streptococcus viridans*, without a vegetation, but with a history of fever, congenital heart disease, and a recent dental procedure. (3) Positive blood cultures for a pathogen, without a vegetation, but with fever and congenital heart disease and no other apparent source of infection. (4) Negative blood cultures for a pathogen, but with fever, congenital heart disease, vascular phenomena, and new valvular regurgitation. (5) Histopathological evidence of endocarditis on tissue obtained at surgery or during autopsy.

2.1. Follow-up

Data on patients preoperative clinical features, operations, clinical course, pathological, microbiological, postmortem findings, late events and survival were obtained through a detailed review of hospital medical records. Additional information was sought from the referring physicians, family doctors and/or the patients’ families as appropriate.

Follow-up was complete for all patients averaging 11.2 years (range 0–26.3 years) with a total of 179.5 patient years.

3. Results

3.1. Preoperative clinical and pathological features

Thirteen patients had native valve endocarditis (NVE) and three prosthetic valve endocarditis (PVE). The aortic valve was infected in five, the mitral in four, both aortic and mitral in one, the tricuspid in four, both tricuspid and pulmonary valves in one and an aortic homograft in one patient (Table 1).

Fever in 12, rigors in six, shortness of breath in six and generalised malaise in seven patients were the most common presenting symptoms being present for a mean duration of 36.9 days (SD 25.4, range 0–135 days).

Events predisposing to endocarditis, were identified in six patients: routine cardiac catheterisation, 5 weeks earlier, in a patient with complete heart block (S. aureus), dental treatment without antibiotic cover, 2 weeks earlier, in a patient with a small ventricular septal defect (*S. epidermidis* in three) and streptococcal species in five patients (*Staphylococcus aureus* in five, *S. viridans* in two).

The mean duration of antibiotic treatment preoperatively was 20.9 days (SD 15.7, range 5–86 days).

Indications for surgery were severe valve dysfunction in nine, cardiac failure in five, vegetations in nine, persistent sepsis in four and embolosis in four patients. Emboli were pulmonary in two and systemic affecting the brain cerebral, sacro-iliac joint, metatarsal bone and lumbar vertebra in three patients.

3.2. Operations and operative findings

All operations were carried out during the acute phase of the disease process with 12 being emergency and four urgent procedures.

Prior to 1978 we used continuous coronary perfusion for aortic and intermittent cross-clamp for mitral valve replacement; subsequently and up to 1995 myocardial protection was achieved with cold crystalloid cardioplegia (St Thomas’s solution). Since then cold blood cardioplegia has been used. Standard operative principles were the debridement of all infected tissues and abscess cavities, meticulous washing of all affected areas with povidone iodine solution (Betadine) and reconstruction of resulting defects using glutaraldehyde treated autologous or bovine pericardium.

A consideration was always given to preserve the affected native valve; if this was not feasible a valve replacement procedure was employed. Ten patients underwent valve replacement with 11 mechanical prostheses, one received an aortic homograft in pulmonary position, three had

<table>
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<th>Table 1</th>
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<td>Type of endocarditis and position of affected valve*</td>
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<tr>
<td>Type of endocarditis</td>
</tr>
<tr>
<td>NVE</td>
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<tr>
<td>PVE</td>
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<td>Total (no. of patients)</td>
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</tbody>
</table>

*AV, aortic valve; MV, mitral valve; TV, tricuspid valve; PV, pulmonary valve; NVE, native valve endocarditis; PVE, prosthetic valve endocarditis.
removal of vegetations and valve repair, whereas in two excision of vegetations only was carried out. Closure of a ventricular septal defect, in four patients, was the commonest concomitant procedure. Types of operative interventions performed are shown in Table 2.

Pathological operative findings included vegetations in 14, cusp perforation in five, annular abscess in five, rupture of the chordae tendinae or papillary muscles in three, involvement by the infection of myocardial tissues in nine, paraprosthetic leak in one and aneurysm of sinus of Valsava in one patient.

Bacteriological examination of the valves, vegetations or other tissue material removed at operation confirmed the presence of the offending microorganism in 11 patients.

Although there was not a uniform protocol regarding the postoperative administration of antibiotic treatment over the 27 years of the study period, patients with positive gramm-stain or culture of the excised valve, annular abscess or more extensive infection were likely to receive at least a 6 weeks course of intravenous antibiotics following their operation. Mean duration of the antibiotic treatment postoperatively was 35.7 days (SD 12.8, range 0–67 days).

### 3.3. Operative mortality and morbidity

There was one operative death (6.25%) in a 25-day-old neonate who had staphylococcal bacteraemia, severely impaired left ventricular function on preoperative echocardiography and undetectable peripheral pulses. He was taken to the theatre in a moribund condition. At operation extensive vegetations from the pulmonary and tricuspid valves, right atrium and ventricle and the main pulmonary artery were removed but discontinuation from cardiopulmonary bypass was not achieved.

Five children developed postoperative complications. These were intermittent complete heart block requiring temporary epicardial pacing in two, transient renal failure in one, chest infection in one, and bilateral pleural effusions in one patient.

### Table 2

<table>
<thead>
<tr>
<th>Type of operation</th>
<th>Number of patients</th>
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<tr>
<td>AVR</td>
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</tr>
<tr>
<td>AVR and reconstruction of the aortic root</td>
<td>2</td>
</tr>
<tr>
<td>AVR, MVR and repair of coarctation of the aorta</td>
<td>1</td>
</tr>
<tr>
<td>MVR</td>
<td>2</td>
</tr>
<tr>
<td>MVR (re-do for PVE)</td>
<td>2</td>
</tr>
<tr>
<td>Insertion of aortic homograft in the pulmonary position (re-do for PVE)</td>
<td>1</td>
</tr>
<tr>
<td>Excision of vegetations from TV and repair</td>
<td>2</td>
</tr>
<tr>
<td>Excision of vegetations from TV</td>
<td>2</td>
</tr>
<tr>
<td>Excision of vegetations from TV and PV and repair</td>
<td>1</td>
</tr>
<tr>
<td>Total number of patients</td>
<td>16</td>
</tr>
</tbody>
</table>

* AVR, aortic valve replacement; MVR, mitral valve replacement; PVE, prosthetic valve endocarditis; TV, tricuspid valve; PV, pulmonary valve.

### 3.4. Thromboembolism, recurrent infection and re-operation

There was one episode of thrombosis of a mechanical aortic valve in a patient with poor compliance to sodium Warfarin. Another patient experienced a thromboembolic event resulting in transient right hemiparesis. The same patient has subsequently had problems in maintaining normal therapeutic levels of the International Normalised Ratio (INR) and was admitted to the hospital with haematuria.

Endocarditis recurred in one patient (6.25%) 11 years following a MVR for prosthetic valve endocarditis. This was managed successfully with a repeat replacement of the infected mitral prosthesis. Actuarial freedom from recurrent endocarditis at 10 and 20 years was 100 and 87.5%, respectively.

Four patients needed seven further surgical interventions with no operative mortality. The first patient developed thrombosis of an aortic mechanical valve 6 years after his operation and was managed with implantation of a biological prosthesis. This has however disintegrated 11 years later necessitating a second re-operation with insertion of a new bioprosthesis. The second patient required a re-replacement of an infected mechanical valve in the mitral position 11 years after the first operation and a second re-operation for paravalvular leak after 12 months. The third patient who had originally extensive abscess formation involving the three sinuses of Valsava underwent, also, two further interventions: 11 months postoperatively for repair of an aneurysm of sinus of Valsava and 3 years later for aortic regurgitation. The fourth patient had left ventricular myocardial necrosis at initial operation and required a re-intervention 8 months postoperatively to repair a left ventricular aneurysm and a leaking mitral prosthesis. Actuarial freedom from re-operation at 10 and 20 years was 76.1 and 60.9%, respectively (Fig. 1).

### 3.5. Long-term survival

There have been two late deaths, one non-cardiac and the second of unknown cause. The first patient, an insulin dependent diabetic, died 15 years after the operation at the age of 30, following his emergency admission into the intensive care unit in a comatose state due to diabetic keto-acido-diss. The second patient died 23 years postoperatively at the age of 39, the circumstances and the causes of her death are not known. Thirteen patients were alive at the end of the study period. Nine were in NYHA class I with the remaining four being in NYHA class II. Actuarial survival, inclusive of operative mortality at 1, 15 and 20 years was 93.7, 93.7 and 78.1% (Fig. 2).

### 4. Discussion

Improvements in the general healthcare over time should
have, perhaps, led to a decrease in the incidence of infective endocarditis in paediatric population, yet in several recent reports this would appear to be increasing ranging from 0.2 to 0.9 cases per 1000 paediatric hospital admissions per year [1,3,12].

Advances in paediatric cardiac surgery over the last three decades, resulting in many infants and children with complex congenital heart disease surviving, and the widespread use of intravenous catheters and pacemakers would account, at least partly, for the growth of the paediatric population more susceptible to infective endocarditis. Patients with untreated congenital cardiovascular abnorm-

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**Fig. 1.** Freedom from re-operation at 10 and 20 years was 73.1 and 60.9% (oblique lines represent 70% confidence intervals).

**Fig. 2.** Actuarial survival, including operative mortality, at 15 and 20 years was 93.7 and 78.1% (oblique lines represent 70% confidence intervals).
The microbiological findings in our series [1–10] were typical with those most frequently reported from elsewhere comprising staphylococcal and streptococcal species. Other pathogens such as Haemophilus influenzae, Escherichia coli, Klebsiella and other gram-negative organisms, Candida albicans, incriminated as the causative organisms previously [1,6,9], were not encountered in our patients. In three patients (23.1%) preoperative and postoperative blood cultures and the microbiological examination of tissues excised at operation failed to reveal the microorganism responsible for the disease process. The clinical, macroscopic and histopathological features, however, were confirmatory of the presence of endocarditis. Although technical details related to the processing of the cultured material may play a role [13], preoperative administration of antibiotics is the most likely explanation for the 13.0–36.6% prevalence of culture-negative infective endocarditis rates reported for infants and children from other centres [2–4].

4.2. Indication for surgical intervention and surgical technique

Since about 80.0–90.0% of children with infective endocarditis, treated solely with conservative treatment, are expected to survive [1,2]; the selection of those qualifying for surgical intervention should be cautious. The indications for surgery in our series: persistent sepsis, cardiac failure, central, pulmonary or peripheral embolism, infection of a prosthetic valve and vegetation are universally accepted [1–10]. The mere presence of large vegetations, however, maybe a source of therapeutic dilemmas. Although echocardiography provides useful information on the size and other morphologic features of vegetations, this information is of little help in predicting the possibility for embolization [2,14]. In our view, the combination of large vegetations with ongoing sepsis is a clear indication for surgical intervention. However if there is clinical evidence of resolution of the infection and no embolic phenomena, a conservative management may be justified, in the hope that the vegetations may also resolve.

Preservation of the native tissues, without compromising the completeness of the clearance of all infected material is highly desirable. In this series this was achieved in five out of 13 patients with native valve endocarditis, by performing excision of vegetations in two and removal of vegetations with valve repair in three. In the remaining eight patients with native and in three with prosthetic valve infection a valve replacement was required. Our experience in this respect would appear to be similar with that reported by others [4,7,10].

4.3. Early outcome

The operative mortality (6.2%) and morbidity (31.3%) rates were relatively low considering the urgent or emergency character of the operations in all 16 cases. The five children who developed moderately severe complications responded well to usual therapeutic measures.

The only peri-operative death occurred in a 25-day-old neonate (the only young infant in this series) with severe staphylococcal septicaemia, poor ventricular function and cardiovascular collapse brought into operating room in a moribund condition. Surgical intervention for endocarditis in the very young children and neonates seems to carry a higher operative risk: in the series of Citak et al. [4] operative mortality rate in children under 2 years of age was 43% compared with 11.0% in patients 2 years of age or older, the only operative death in the report by Horvath et al. [7] was recorded in a 2-month-old baby whereas two neonates comprised the only operative fatalities amongst 14 patients described by Tolan et al. [8].

The operative mortality reported by other centres varies between 0 and 50.0% (Table 3). Since, however, the numbers of the patients included in all series are small and the differences in the peri-operative death rate are likely to reflect, at least partly, the variable make up of the patients involved, comparisons should be made cautiously. So, in considering the 50.0% early mortality in series of Schollin et al. [6], one should bear in mind that there were only six patients involved and two out of three operative deaths occurred in 2- and 3-week-old neonates having fungal infection. Meaningful comparison of the outcome following medical versus combined medical and surgical treatment, on the other hand, cannot be undertaken since the children referred for surgery constitute a far higher risk group.
4.4. Late outcome

Eradication of the infective focus, repair of the resulting defects and restoration of haemodynamic stability with the least possible undesired early and late side effects are the main goals of surgery for infective valvular endocarditis.

The 6.2% re-infection rate at a mean follow-up of 11.2 years with an actuarial estimate of freedom from recurrence of 100.0 and 87.5% at 10 and 20 years is rewarding. Our experience would, thus, suggest that adequate debridement of the infected tissues, washing of the affected areas with povidone iodine solution, repair of the resulting defects with glutaraldehyde treated autologous or bovine pericardium and implantation of mechanical prostheses can result in a lengthy freedom from recurrent infection.

The use of homografts for aortic valve or root infection has been associated with significantly lower early re-infection rate in comparison with mechanical valves and bioprostheses [15]. Homografts have, in addition, the merit of not requiring anticoagulation and exhibit good haemodynamic characteristics. However, they have the problems of accelerated calcification, particularly in young children, limited durability and availability and they may need multiple further replacements [16]. Modern mechanical low profile bileaflet valves perform well in the aortic position, have long durability and can be remarkably resistant to re-infection [17]. The need for anticoagulation and the risk of thromboembolism are significant problems, but, provided the facilities for meticulous monitoring are available, anticoagulants in children seem to be well tolerated [18].

In this series there were only five children who might have been considered, by others, for homograft aortic valve replacement, but none of them was an infant, an age group where the performance of a Ross procedure may be, indeed, indicated.

We currently favour the use of homografts for invasive forms of aortic root infection in adults but prefer mechanical prostheses for irreparable valvular lesions in children [17,18].

The 25.0% re-operation rate, related partly to the anatomical changes induced by the infection, and the prediction of a re-operation rate of 39.0% at 20 years (Fig. 1), indicates that there is a continuous re-operation hazard for the children with infective valve endocarditis even though they underwent a successful initial surgical treatment.

It is encouraging, nevertheless, that the re-operations, by not causing any operative mortality, have contributed to the good long-term survival, with 13 amongst the 15 hospital survivors remaining alive having an actuarial estimate of 15-year survival of 93.7% (Fig. 2).

The information available on the late outcome (recurrent infection, re-operation and survival) for surgically treated children and neonates in other reports is sparse. Citak et al had only one late death amongst 11 hospital survivors with an up to 10 years follow-up [4], all ten patients were alive in the series of Horvath et al., with a maximum follow-up of 8 years (median 39 months) [7], Picarelli et al. reported a re-operation rate of 17% and no late deaths amongst 18 patients (out of 21 hospital survivors) followed up for a maximum of 9 years (mean 3.8 years) [10] whereas Nomura et al. described a re-infection rate of 13.4% and four late deaths, amongst 28 hospital survivors, and an actuarial 10 years survival of 76.0% with a maximum follow-up of 10 years [5].

5. Conclusion

Surgery for infective valve endocarditis in children can be performed with low mortality; our experience and the other published evidence would, nevertheless, suggest that in the neonates and the youngest paediatric patients this may be substantial.

Meticulous application of standard operative principles and implantation of mechanical prostheses, in this series, provided lasting freedom from re-infection.

Although a considerable number of patients may require further surgical interventions, the long-term survival is most satisfactory.

References