Surgery for paravalvular abscess in children.

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PII: S2666-2736(23)00330-3
DOI: https://doi.org/10.1016/j.xjon.2023.08.027
Reference: XJON 930

To appear in: JTCVS Open

Received Date: 14 May 2023
Revised Date: 13 August 2023
Accepted Date: 28 August 2023


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Surgery for paravalvular abscess in children

Methods

- A retrospective analysis of all patients at a single institution who underwent surgery for paravalvular extension of infective endocarditis between 1989 and 2020 was performed.

Results

- *Streptococcus pneumoniae* (HR 9.2, 95%CI 1.6–51.7) and preoperative shock (HR 6.4, 95%CI, 1.3–32.0) were associated with mortality.
- Central fibrous body reconstruction was associated with reoperation (HR 4.4, 95%CI, 1.2–16.1).

Conclusions

- Paravalvular abscess in children is associated with high early mortality.
- Hospital survivors, however, have good long-term survival.
- Reoperation is frequent but is rarely due to recurrence of endocarditis.
Surgery for paravalvular abscess in children.

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Words: 2725

Key Words: Paravalvular abscess, Infective endocarditis, Cardiac surgery, Children

Presented at the AATS 103rd Annual Meeting, May 6th-9th, 2023, Los Angeles, CA.

Funding and Disclosures: Dr. Wu is a recipient of an Australian Government Research Training Program Scholarship. Dr. Zhu is a recipient of an Australian Government Research Training Program Scholarship, a National Health and Medical Research Council (NHMRC) Postgraduate Scholarship (APP2013821), a National Heart Foundation PhD Scholarship (106284), and an Early Career Research Scholarship from the Avant Foundation (2021/164).

Conflict of Interest: Prof. Brizard serves on the advisory board of Admedus. No other disclosures.

Ethics: Ethics approval was obtained from the Human Research Ethics Committee at the Royal Children’s Hospital, Melbourne, Australia (No. 36250A) on the 30th of August, 2016.

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CENTRAL MESSAGE
Despite high early mortality, surgery for paravalvular abscess is effective, with hospital survivors demonstrating good long-term survival, often without recurrence of endocarditis.

**PERSPECTIVE**

Paravalvular abscess often necessitates complex surgical techniques, which have been associated with high operative mortality and persistent infection in adults. Evidence on outcomes of surgery in children is limited. Our results demonstrate good long-term survival and few instances of recurrence. However, early mortality is high and reoperations are frequent.

**ABBREVIATIONS AND ACRONYMS**

RV-PA = right ventricle to pulmonary artery

ECMO = extracorporeal membrane oxygenation

TEE = transesophageal echocardiography

**ABSTRACT**
Objective: We investigated the outcomes of surgery in children with paravalvular abscess at our institution.

Methods: A retrospective review of all patients who underwent surgery for paravalvular abscess was performed.

Results: Between 1989 and 2020, 30 patients underwent surgery for paravalvular abscess, of whom 16.7% (5/30) had an intracardiac fistula and 20.0% (6/30) had a pseudoaneurysm. Aortic annulus abscesses were most common, occurring in 76.7% (23/30). Aortic root replacement was performed in 56.7% (17/30), root reconstruction was performed in 13.3% (4/30), and reconstruction of the central fibrous body was required in 16.7% (5/30). Postoperatively, 23.3% (7/30) required extracorporeal membrane oxygenation (ECMO) support, and 3.3% (1/30) required permanent pacemaker insertion. There were 6 early deaths, 5 of whom were on ECMO, and no late deaths, with survival being 79.7% (95% CI, 60.2-90.3) at 15 years. Deaths occurred due to sudden cardiac arrest resulting in brain death in 3 patients, an inability to wean ECMO due to severe cardiac dysfunction in 2 patients, and cerebral mycotic aneurysm and hemorrhage in 1 patient. Freedom from reoperation was 40.0% (95% CI, 17.0-62.3) at 15 years. Reoperation due to recurrence was rare, occurring in 6.7% (2/30). *Streptococcus pneumoniae* (HR 9.2, 95% CI 1.6-51.7) and preoperative shock (HR 6.4, 95% CI, 1.3-32.0) were associated with mortality. Central fibrous body reconstruction was associated with reoperation (HR 4.4, 95% CI, 1.2-16.1).

Conclusions: Although paravalvular abscess in children is associated with high early mortality, hospital survivors have good long-term survival. Reoperation is frequent but is rarely due to recurrence of endocarditis.

INTRODUCTION
Paravalvular extension of infective endocarditis, including annular abscess, pseudoaneurysm and intracardiac fistula formation, is a challenging complication requiring urgent surgical management. Given the extensive destruction of tissue, complex reconstructive techniques are often required. In adults, operative mortality is high and infections may persist despite surgical intervention. In children, however, outcomes of surgery for paravalvular abscess are poorly described, with surgical guidelines and approaches based upon those for adults. Therefore, we sought to investigate the outcomes of surgery in children with infective endocarditis with paravalvular extension at our institution.

**MATERIALS AND METHODS**

This study was approved by the Human Research Ethics Committee at the Royal Children’s Hospital, Melbourne, Australia (No. 36250A) on the 30th of August, 2016. All patients who underwent surgery for infective endocarditis with paravalvular extension between 1989 and 2020 were included. Patients were identified if they demonstrated evidence of paravalvular extension, including abscesses, pseudoaneurysms and intracardiac fistulae, on preoperative echocardiography or intraoperatively. Data were retrospectively obtained from medical records. Follow-up was obtained by reviewing correspondence from a patient’s general practitioner or cardiologist, providing information on their current status.

**Definitions**

Early mortality or early reoperation were defined as death or reoperation within 30 days of surgery or before initial hospital discharge, respectively. All other deaths or reoperations were considered late.
Diagnosis of infective endocarditis was dated as the time when the patient initially met the Duke Criteria or the start date of intravenous antibiotic administration, whichever occurred first.

**Statistical Analysis**

All data were analyzed using Stata MP, version 16 (StataCorp LLC, College Station, TX). Categorical variables are expressed as n (%) and compared using the \( \chi^2 \) test or Fisher’s exact test if group size was <10. Continuous variables are expressed as median with interquartile range (IQR). Kaplan-Meier survival curves were used to analyse time-related end points. Cox regression analyses were used to identify relationships between variables. A \( P \)-value <0.05 was considered statistically significant.

**RESULTS**

Between 1989 and 2020, 30 patients underwent surgery for paravalvular abscess, of whom 16.7% (5/30) had an intracardiac fistula and 20.0% (6/30) had a pseudoaneurysm. Aortic annulus abscesses were most common, occurring in 76.7% (23/30). Mitral annulus abscesses occurred in 16.7% (5/30), right ventricle to pulmonary artery (RV-PA) conduit abscesses occurred in 6.7% (2/30), and tricuspid annulus abscesses occurred in 3.3% (1/30).

Baseline characteristics are detailed in Table 1. Median age was 7.6 years (IQR, 1.2-12.6), median height was 123cm (IQR, 80-155) and median weight was 22.6kg (IQR, 10.8-39.8).

**History of Congenital Heart Disease**

Congenital heart disease was present in 70.0% (21/30) of patients. Aortic stenosis and bicuspid aortic valves were most common, occurring in 23.3% (7/30) each, followed by ventricular septal defect in 13.3% (4/30), truncus arteriosus and patent foramen ovale in
10.0% (3/30) each, and Ebstein’s anomaly, patent ductus arteriosus, double outlet right ventricle and pulmonary atresia in 3.3% (1/30) each. Previous cardiac surgery was performed in 43.3% (13/30), 4 of whom had previous valve replacement, and 26.7% (8/30) had intracardiac prosthetic material present prior to surgery for paravalvular extension of infective endocarditis.

**Microbiology**

There were 26 (86.7%, 26/30) positive blood or tissue cultures. Gram positive organisms were most commonly isolated, occurring in 92.3% (24/26) of positive cultures. *Staphylococcus aureus* was isolated from 33.3% (10/30) of patients, where 9 cultures grew methicillin-sensitive *Staphylococcus aureus* and 1 grew methicillin-resistant *Staphylococcus aureus*.

Streptococci were also common with *Streptococcus viridans* grown in 13.3% (4/30), *Streptococcus pneumoniae* in 10.0% (3/30), coagulase-negative staphylococci and Group B streptococci in 6.7% (2/30) each, *Streptococcus mitans* in 3.3% (1/30), and other streptococci species in 3.3% (1/30).

*Corynebacterium* and *Kingella* were cultured from 6.7% (2/30) patients each, while *Pseudomonas*, *Klebsiella* and *Enterococcus* were isolated from 1 patient (3.3%, 1/30) each.

**Preoperative Course**

The majority of patients (96.7%, 29/30) presented acutely septic with fevers or an elevated serum C-reactive protein level. The remaining patient presented with acute heart failure. A third of patients required preoperative intensive care admission due to heart failure, with 16.7% (5/30) admitted for cardiogenic shock. All patients had large intracardiac lesions or intracardiac fistulae on imaging, which, together with their clinical presentation, was
concerning for abscess formation, prompting consideration for urgent surgery. Median time from diagnosis to surgery was 3.0 days (IQR, 1.0-7.3).

Complications of heart failure occurred in 43.3% (13/30) of patients, leaflet perforation in 33.3% (10/30), and cardiogenic shock in 16.7% (5/30).

Embolization occurred in 30.0% (9/30) with cerebral embolization occurring in 10.0% (3/30), musculoskeletal embolization in 26.7% (8/30), splenic embolization in 6.7% (2/30) and renal embolization in 10.0% (3/30). Neurological symptoms due to cerebral embolization were present in 2 patients (6.7%, 2/30). No patients required preoperative dialysis.

On preoperative echocardiography, the majority of patients (93.3%, 28/30) had valve regurgitation preoperatively. Over half (53.3%, 16/30) of patients had moderate or greater aortic regurgitation on latest preoperative echocardiography, while 20.0% (6/30) had moderate or greater mitral regurgitation, and 6.7% (2/30) had moderate or greater tricuspid regurgitation.

**Operative Technique**

Operations performed and their associated outcomes are summarised in Table 2.

Aortic root replacement was performed in 56.7% (17/30), with 9 patients (30.0%, 9/30) undergoing homograft root replacement and 8 patients (26.7%, 8/30) undergoing a Ross procedure. Aortic root reconstruction was performed in 13.3% (4/30). Mechanical aortic valve replacement was performed in 3 patients (10.0%, 3/30).

Concomitant reconstruction of the central fibrous body was required in 16.7% (5/30).
There were 5 mitral annulus abscesses, where 3 patients (60.0%, 3/5) underwent mitral valve repair and 2 patients (40.0%, 2/5) underwent mitral valve replacement, one with a mechanical valve and the other with a bioprosthetic valve. Mitral valve repair was performed through abscess debridement and annuloplasty in 1 patient, ring annuloplasty and neochordae formation in 1 patient, and abscess debridement in 1 patient.

One patient (3.3%, 1/30) with a tricuspid annulus abscess underwent a tricuspid valve repair involving annulus resection and ring annuloplasty.

There was involvement of previously inserted RV-PA conduits in 2 patients (6.7%, 2/30), requiring RV-PA conduit replacement. One RV-PA conduit replacement was performed concomitantly with a homograft aortic root replacement.

**Postoperative Course**

Postoperatively, 23.3% (7/30) required extracorporeal membrane oxygenator (ECMO) support, and 3.3% (1/30) required permanent pacemaker insertion following deliberate resection of infected conduction tissue. Of those requiring ECMO support, 2 patients (40.0%, 2/5) had undergone reconstruction of the central fibrous body. Heart block occurred in 1 patient (3.3%, 1/30) postoperatively, which resolved, and in 2 patients (6.7%, 2/30) who had early deaths. Two patients (6.7%, 2/30) required a brief period of peritoneal dialysis. There were 6 patients with postoperative embolization, 5 of which were cerebral (83.3%, 5/6) and 1 of which was pulmonary (1/6, 16.7%).

**Mortality**
There were 6 early deaths, 5 of which were on ECMO prior to deaths, and no late deaths, with survival being 79.7% (95%CI, 60.2-90.3) at 5, 10 and 15 years (Figure 1A). Deaths occurred due to sudden cardiac arrest resulting in brain death in 3 patients, an inability to wean off ECMO due to severe cardiac dysfunction in 2 patients, and cerebral mycotic aneurysm and hemorrhage in 1 patient.

On Cox regression analyses, Streptococcus pneumoniae (HR 9.2, 95%CI 1.6-51.7) and preoperative shock (HR 6.4, 95%CI, 1.3-32.0) were independently associated with mortality.

There were 2 deaths (25.0%, 2/8) in those who underwent a Ross procedure, and 3 deaths (37.5%, 3/8) in those who underwent a homograft root replacement. One death (33.3%, 1/3) occurred in a patient undergoing a mechanical aortic valve replacement for an aortic root abscess, with concomitant mitral valve replacement and central fibrous body reconstruction. In patients who underwent central fibrous body reconstruction, there were 2 deaths (40%, 2/5), following a period of ECMO support in both cases.

There were no deaths amongst those with mitral annulus, tricuspid annulus, and RV-PA conduit abscesses.

**Freedom from Reoperation**

Freedom from reoperation was 60.6% (95%CI, 38.9-76.7) at 5 years, 50.0% (95%CI, 28.3-68.4) at 10 years, and 40.0% (95%CI, 17.0-62.3) at 15 years (Figure 1B).

There were 5 early reoperations (16.7%, 5/30) due to an aneurysmal dilation of the aortic root in 1 patient, revisions of the aortic and mitral prostheses in 1 patient, development of vegetation in the RV-PA conduit in 1 patient, development of a ventricular pseudoaneurysm in 1 patient, and right heart failure in 1 patient.
There were 14 late reoperations in 8 patients. There were 8 aortic valve replacements, 7 of which were mechanical valve replacements and 1 of which was a Ross procedure, due to worsening aortic stenosis or regurgitation. There were 4 patients who underwent reoperation following an initial homograft root replacement, where 3 patients underwent a further mechanical valve replacement and 1 patient underwent a further Ross procedure. This was due to progressive valve deterioration in 3 patients, and acute onset valve regurgitation due to recurrence of endocarditis in 1 patient. In contrast, there were 2 reoperations in those who underwent an initial Ross procedure, one due to annular dilation and the other for conduit stenosis.

Mitral valve repair was required in 1 patient due to progressive annulus dilation following an initial homograft aortic root replacement and mechanical mitral valve replacements were required twice in 1 patient, due to culture-negative infective endocarditis in the initial replacement, occurring concomitantly with a mechanical aortic valve replacement, and mitral stenosis in the following replacement. There were 2 pulmonary valve replacements, due to right ventricular outflow tract dilation and pulmonary stenosis, respectively, and 1 RV-PA conduit replacement.

Reoperation due to recurrence of infective endocarditis was rare, occurring in 6.7% (2/30). Freedom from reoperation due to recurrence was 91.1% (95%CI, 68.9-97.7) at 5, 10 and 15 years (Figure 1C).

In those undergoing homograft root replacement, there were 5 reoperations overall (55.6%, 5/9), whilst in those undergoing a Ross procedure, there were 2 reoperations overall (25.0%, 2/8). This difference, however, did not reach statistical significance.
Late reoperations were required in 60.0% (3/5) of patients undergoing reconstruction of the central fibrous body and on Cox regression analyses, this was a predictor of reoperation (HR 4.4, 95%CI, 1.2-16.1).

Of patients with mitral annulus abscesses, 1 patient, who underwent an initial valve replacement with a bioprosthetic valve, required a late redo mitral valve replacement for mitral stenosis, followed by a mechanical aortic valve replacement.

Reoperations were not required in those with a tricuspid annulus abscess or RV-PA conduit abscess.

**Follow-up**

Follow-up was complete for 95.8% (23/24) of the 24 surviving patients. The median follow-up time was 9.25 years (IQR, 2.8-17.7). Of these patients, 75.0% (18/24) of patients were in New York Heart Association (NYHA) class I at late follow-up. Ongoing neurological deficits were reported in 8.3% (2/24) of patients. No patients required dialysis on late follow-up.

**DISCUSSION**

Despite significant associated morbidity and mortality, there are few reports on the surgical management of paravalvular abscess in children. Therefore, recommendations for treatment of these children are largely derived from adult guidelines. This study aims to further demonstrate the outcomes of surgery for paravalvular abscess in children. A graphical abstract of this study is presented in Figure 2.

Early mortality was high in our cohort (20.0%, 6/30), as expected, given both the extent of infection and surgical complexity. This is consistent with reports in adults, with
operative mortality of 15.5% reported by David and colleagues and 13% reported by d’Udekem and colleagues. In contrast, the long-term survival was excellent with no late deaths, and the majority of patients were in NYHA class I at late follow-up.

Only one other report by Chaturvedi and colleagues described children undergoing surgery for aortic root abscess, describing similar results to the current study. In a cohort of 5 children who all underwent a homograft aortic root replacement, there was 1 early death (20.0%, 1/5) and all 4 surviving children were in NYHA I at final follow-up.

Reoperations were frequently required but few were due to recurrence of endocarditis. In adults, d’Udekem and colleagues reported survival of 64% and freedom from recurrent endocarditis of 76% at 8 years following radical resection of the abscess and any infected or inflamed tissue. Similarly, Spiliopolous and colleagues demonstrated that radical surgical management was associated with acceptable mortality, and in their cohort, no recurrence of endocarditis. Based on our results, radical resection of all infected tissue yields similar outcomes in children. This approach likely ensures complete removal of the infective source, facilitating recovery in the septic child and reducing the risk of reinfection. Moreover, the acceptable late survival rates both in adults and in our cohort of children suggests that a radical approach is effective in the management of paravalvular abscess.

In particular, reconstruction of the central fibrous body or aortomitral curtain, also known as the Commando procedure, is an approach necessary in only the most extensive cases of disease. Previous reports in adults have demonstrated high operative mortality and satisfactory long-term survival, freedom from reoperation and recurrence. In our cohort of children, a third of early deaths occurred in those requiring ECMO support, following a Commando procedure. There were no late deaths but 60.0% (3/5) required late reoperation.
The Commando procedure was identified as a risk factor for reoperation. Although early mortality was high likely due to both the severity of infection and invasive nature of the procedure, these results further reinforce the efficacy of radical resection in hospital survivors.

Preoperative shock was associated with an increased risk of mortality, as expected. *Staphylococcus aureus* was the most commonly isolated microorganism but was not found to be significantly associated with mortality. *Streptococcus pneumoniae*, however, was a predictor for death, and has previously been described as a cause of rapidly progressive endocarditis and mortality.9-11

Heart block has been described as a common complication of paravalvular abscess due to the mass effect on conduction tissue of an enlarging abscess.12,13 In our group, no patients were identified as having heart block preoperatively. Postoperatively, only 1 patient required permanent pacemaker insertion, demonstrating that extensive reconstructive surgery does not necessarily result in complete heart block. This may be attributed to our preference for early identification of abscess and early surgery, with a median time from diagnosis to surgery of 3 days, before the abscess encroaches upon conduction tissue. Transesophageal echocardiography (TEE) has previously been described as being able to more accurately identify paravalvular abscess than transthoracic echocardiography.14 Therefore, at our institution, patients suspected of having infective endocarditis are routinely screened with TEE preoperatively, allowing for early identification of paravalvular extension. Urgent surgery in acutely septic children with infective endocarditis has also been shown to be safe and appears to carry a lower risk compared to adults, resulting in moves towards earlier intervention.15-18 Chaturvedi and colleagues5 adopted a similar approach of operating urgently, with all 4 surviving patients in sinus rhythm at late follow-up.5 It is possible that
early intervention reduces the risk of complete heart block by limiting the extent of tissue destruction.

The Ross procedure has become an increasingly attractive option in children due to its somatic growth potential and resistance to infection.\textsuperscript{19} Although there have been concerns about the feasibility of the Ross procedure in sepsis given its technical complexity,\textsuperscript{5,20} We have recently shown the Ross procedure as the preferred alternative in children with infective endocarditis when aortic valve repair is not feasible; recurrence was rare and the Ross procedure was shown to be superior to homograft root replacement with respect to freedom from reoperation.\textsuperscript{21} In our present study, mortality is comparable between the Ross procedure and homograft root replacement whilst reoperations appear to be more prevalent amongst the homograft group, although this did not reach statistical significance. It appears, then, that the Ross procedure may be the preferred option for aortic root replacement in children presenting with paravalvular abscess.

There are few reports on mitral annulus, tricuspid annulus, and RV-PA conduit abscesses in both adults and children. In our limited subset of these patients, long-term postoperative outcomes appear acceptable. Notably, the only patient requiring reoperation had received a bioprosthetic mitral valve, which may explain their need for reoperation. We have also previously shown that mitral valve repair is feasible in the majority of cases of pediatric infective endocarditis, and it is reassuring that despite annular involvement, repair was possible in over half of the cases in our cohort.\textsuperscript{16}

\textbf{LIMITATIONS}
This study is primarily limited by its relatively small sample size with few adverse outcomes over a large time period. Statistical analysis, therefore, may not have properly identified all associations between variables. Moreover, due to further reductions in sample size and outcomes, analyses of specific subgroups such as those with aortic root abscesses did not generate any meaningful results.

CONCLUSIONS

Although paravalvular abscess in children is associated with high early mortality, hospital survivors have good long-term survival. Reoperation is frequent but is rarely due to recurrence of endocarditis.
REFERENCES


### Table 1. Baseline demographic of patients (N=30)

Values are presented as n (%) or median (interquartile range).

<table>
<thead>
<tr>
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</thead>
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<td><strong>Height (cm)</strong></td>
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<tr>
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<tr>
<td>Operation</td>
<td>Result</td>
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<tr>
<td>-----------------------------------</td>
<td>--------</td>
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<tr>
<td>Homograft aortic root replacement</td>
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<td>Ross procedure</td>
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<tr>
<td>Reconstruction of the central fibrous body</td>
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<td>Aortic root reconstruction</td>
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<tr>
<td>RV-PA conduit replacement</td>
<td>2 (6.7)</td>
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<tr>
<td>Tricuspid valve repair</td>
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</tr>
</tbody>
</table>

**Table 2. Operations performed and associated outcomes (N=30)**

Values are presented as n (%) or median (interquartile range).

**Figures**
Figure 1. Kaplan-Meier curves for (A) overall survival, (B) freedom from reoperation, and (C) freedom from reoperation due to recurrence of endocarditis.

Figure 2. Graphical abstract

Central Figure: Surgery for paravalvular abscess is associated with high early mortality but good long-term survival
Surgery for paravalvular abscess in children

Methods

- A retrospective analysis of all patients at a single institution who underwent surgery for paravalvular extension of infective endocarditis between 1989 and 2020 was performed.

Results

- Streptococcus pneumoniae (HR 9.2, 95%CI 1.6–51.7) and preoperative shock (HR 6.4, 95%CI, 1.3–32.0) were associated with mortality.
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