Outcomes of Surgical Therapy for Infective Endocarditis in a Pediatric Population: A 21-Year Review

Hyde M. Russell, MD, Soraya L. Johnson, BS, Katherine C. Wurlitzer, BA, and Carl L. Backer, MD

Division of Cardiovascular-Thoracic Surgery, Ann & Robert H. Lurie Children's Hospital of Chicago, and Department of Surgery, Northwestern University, Feinberg School of Medicine, Chicago, Illinois

Background. **Infective endocarditis is a rare disease in the pediatric population. We sought to define patient characteristics and outcomes of surgical therapy for endocarditis in children.**

Methods. **We performed a retrospective review of all patients with infective endocarditis who received surgical therapy between January 1, 1990, and March 1. 2011. We were interested in their congenital heart defect, prior surgical procedures, and outcome of the operation.**

Results. **We identified 35 cases of endocarditis in 34 patients requiring surgical intervention. Mean age was 10.7 ± 8.8 years. There was a bimodal age distribution at presentation: 11 (31%) were younger than 1 year and 15 (43%) were 10 to 21 years. Of the 34 patients, 22 (63%) had no history of prior cardiac operation. The infective organism was identified in 30 (86%), with *Staphylococcus aureus* (n = 8) and *Streptococcus viridans* (n = 6) predominating. Valve replacement was performed in 22 patients and valve repair in 10. All patients received 6 weeks of postoperative intravenous antimicrobial therapy. Operative mortality was 15% (5 of 34). The 5 deaths occurred in infants who were a mean age of 2.5 months, and 3 of the 5 infants (60%) were premature. Of 4 patients with fungal infection, 3 patients died. The Ross operation was performed successfully in 5 patients with severe aortic valve disease. Reoperations (n = 10 [28%]) included valve replacement in 5 and conduit replacement in 3, all but 1 due to somatic growth resulting in functional stenosis.**

Conclusions. **The outcome of surgical therapy for endocarditis in children was similar to that reported for adults, with an overall mortality of 15%. The Ross operation was very effective in patients with aortic valve endocarditis. There is a significant incidence of late reoperation for valve and conduit replacement due to somatic growth. Age younger than 1 year, prematurity, and fungal organisms appear to be risk factors for death. Patients surviving to discharge had good outcomes, with no episodes of recurrent endocarditis.**

(Ann Thorac Surg 2013;96:171–5)

Infective endocarditis (IE) is a rare condition in children, with potentially serious consequences. The complex nature of the disease demands an accurate diagnosis and prompt treatment, which may include surgical intervention. Understanding the population at risk is imperative to prevention efforts. In contrast to the adult population, relatively little is reported about this disease in the young. The yearly incidence is estimated to be between 0.34 and 0.64 cases per 100,000 children based on large population samples [1–3]. We sought to characterize those children who required surgical intervention for IE in our institution from 1990 to 2011, with a focus on anatomic location, organisms, and outcomes.

Material and Methods

Our Institutional Review Board approved this study and waived the need for individual consent.

All patients undergoing cardiac operations for endocarditis at our institution between January 1, 1990, and March 1, 2011 were identified from our surgical database. The demographic characteristics and fundamental congenital heart defect (if any) were cataloged. The etiologic organism, if known, was identified from microbiology culture data and recorded. Operative details and surgical outcomes, including need for reoperation, were obtained from the medical record.

Results

We identified 35 cases of endocarditis in 34 patients (63% male) who required surgical intervention during the study

Accepted for publication Feb 12, 2013.

Presented at the Fifty-ninth Annual Meeting of the Southern Thoracic Surgical Association, Naples, FL, Nov 7–10, 2012.

Address correspondence to Dr Russell, Division of Cardiovascular-Thoracic Surgery, Ann & Robert H. Lurie Children's Hospital of Chicago, MC 22, 225 E Chicago Ave, Chicago, IL 60611; e-mail: hrussell@luriechildrens.org.

0003-4975/$36.00
http://dx.doi.org/10.1016/j.athoracsur.2013.02.031

period. This represents less than 1% of all open heart cardiac surgical cases occurring during the same time. The cohort was a mean age of 10.7 ± 8.8 years. There was a bimodal age distribution at presentation with 11 (31%) being infants younger than 1 year, 4 (11%) between 1 and 10 years, 15 (43%) adolescents between 10 and 21 years, and 4 patients (11%) who were older than 21 years (Fig 1).

Cardiac anatomy was normal in 40% of the cohort, and 60% were born with a congenital heart defect. For purposes of this study, patients with nonregurgitant bicuspid valves without significant valvar or left ventricular outflow tract obstruction were considered "normal" anatomy. Thirty-seven percent of the patients had undergone prior cardiac operations. Fundamental diagnoses are listed in Table 1.

The causative microbiologic organism was identified in 86% of the patients. *Staphylococcus aureus* and *Streptococcus viridans* predominated, at 23% and 17%, respectively. Fungal endocarditis (n = 4) represented 11% of cases, all occurring in infants (Fig 2).

Anatomically, the mitral valve was affected most often (45%), followed by the aortic valves (37%) and the tricuspid valves (18%; Table 2). The native valves were involved in 78% compared with prosthetic valves in 22%. Mitral operations consisted of repair in 7 patients by means of leaflet and vegetation excision with autologous pericardial patch reconstruction. Five patients required mitral valve replacement.

Aortic valve endocarditis occurred in 10 patients. Surgical intervention included aortic valve replacement in 3, valve and root replacement in 2, and a Ross operation in 5. Tricuspid valve IE occurred in 5 patients and was treated by repair in 3 and replacement in 2. No IE occurred on native pulmonary valves. Endocarditis developed in 5 patients with right ventricular outflow tract conduits from previous operations, for an incidence of 0.09% of the 521 conduits implanted in our institution during the study period. Underlying diagnoses included tetralogy of Fallot in 3 patients, a history of a Ross operation in 1, and complex 2-ventricle repair of heterotaxy in 1. One of these patients had undergone a Ross procedure for native aortic valve endocarditis and then pulmonary homograft endocarditis developed 4 years later. Although both organisms were *Streptococcus* spp, this second episode developed after a dental procedure

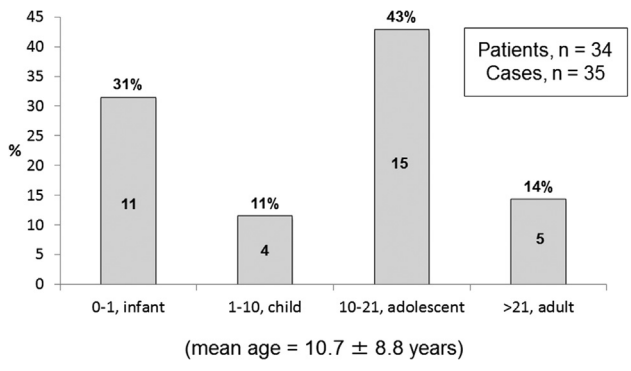

Fig 1. Age distribution of patients in the study population.

Table 1. Cohort Characteristics

Diagnosis	No. (%)
Normal cardiac anatomy	14 (40)
Congenital cardiac anomaly	21 (60)
Ventricular septal defect	5 (14)
Atrioventricular septal defect	4 (11)
Transposition of the great arteries	4 (11)
Tetralogy of Fallot	3 (9)
Pulmonic stenosis	2 (6)
Functionally univentricular heart	1 (3)
Subaortic stenosis	1 (3)
Coarctation of the aorta	1 (3)

and was judged to be a new infection, distinct from the original infection. Four conduits were pulmonary homografts, and 1 was a Contegra conduit (Medtronic, Minneapolis, MN). Average time to infection was 3.4 years after implant.

Five patients died after the operation. All deaths occurred in infants, 60% of whom were premature. Fungal endocarditis was present in 3 of the 5 nonsurvivors. Reoperations after the endocarditis operation occurred in 10 patients at an average time to reoperation of 5 years. The most common reason for reoperation was prosthetic mitral valve dysfunction, followed by conduit stenosis (Table 3).

Comment

IE is a rare but serious condition in children. This study characterizes the patients in our institution who required surgical treatment. The demographic features of our patients correlate well with a recent national review of the Healthcare Cost and Utilization Project's Kids' Inpatient Database (KID) of 1,588 endocarditis admissions [4], suggesting that the outcomes of this small series are likely representative of those found in similar institutions. The results highlight several important facets in regards to the

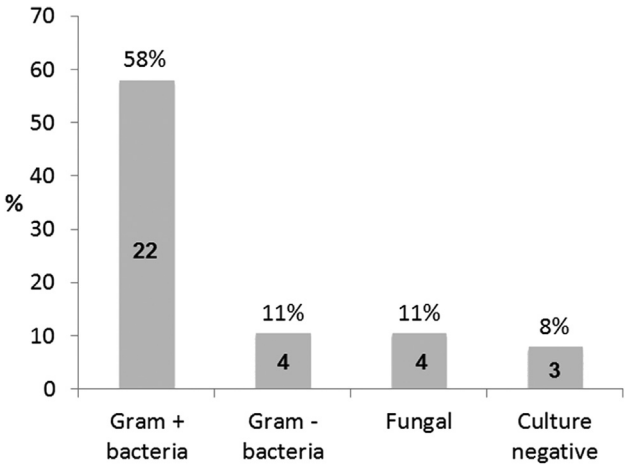

Fig 2. The causative organism, which was identified in 86% of the cases, included Staphylococcus aureus *in 23% and* Streptococcus viridans *in 17%.*

Table 2. Operative Procedures Performed

Type of Surgical Intervention	No. (%)
Mitral	12 (34)
Repair	7
Replacement	5
Aortic	10 (29)
Replacement	3
Root replacement	2
Ross operation	5
Tricuspid	5 (14)
Repair	3
Replacement	2
RV-PA conduit	5 (14)
Other	3 (9)
VSD closure	2
Right atrial mass resection	1
Total	35

PA = pulmonary artery; RV = right ventricle; VSD = ventricular septal defect.

underlying lesion and the microbiologic organism responsible for the disease.

The bimodal age distribution in our study mirrors that of our broader surgical population, with peaks in infancy and adolescence, similar to that reported by others [4, 5]. It is notable that all of the tricuspid endocarditis occurred in infants, presumably secondary to indwelling central venous catheters in long-term hospitalized children. The heightened awareness of central catheter risks may well change this demographic in the future.

Most of our patients had no prior cardiac operations. However, among those who had not undergone operations, one-third carried a diagnosis of congenital heart disease, making congenital heart disease a clear risk factor for the development of IE, in agreement with other reports [6].

Staphylococcus aureus and *Streptococcus viridans* were the most common organisms isolated, and gram-positive bacteria accounted for 58% of the cases. Fungal endocarditis in our study was relegated to the infant population. This finding agrees with previous reports documenting it to be a disease predominantly of patients younger than 1 year [7]. Presumably, chronic indwelling venous catheters, long-term hospitalizations with frequent broad-spectrum antibiotic usage, and relatively immature immune systems are contributing factors [8]. It is important to note how lethal fungal endocarditis was in our study, with 75% of the patients with fungal endocarditis not surviving to discharge.

Our surgical approach to valvar endocarditis is to debride all infected tissue and then reconstruct as necessary. Mitral repair with excision and autologous pericardial patch reconstruction is preferred over replacement, but it is worth noting that compared with replacement, an equal percentage required reoperation. A similar outcome was observed by Hickey and colleagues [9] in a recent report from Toronto, with 3 of 7 mitral repairs requiring eventual reoperation for replacement after endocarditis operations.

Bicuspid valves are overrepresented in those with aortic valve disease, accounting for 50% of that group, despite being present in only 1% to 2% of the population [10]. Although aortic valve repair has been advocated by some [9], we and others [11] have found the results suboptimal. If the aortic valve requires replacement, our current approach in children and young adults is a Ross operation. The efficacy of this procedure in the setting of endocarditis has been noted by other groups as well [12–14]. Given that the entire root will be replaced, there is never compromise in debriding aortic tissue, and the operation is especially effective for patients with annular or root abscesses.

The right ventricular outflow tract conduit is unique to the congenital heart surgical population. Day and colleagues [4] hypothesized that these conduits were a contributing factor among the high death rate found in patients with tetralogy of Fallot and pulmonary atresia in the nationwide KID database study of endocarditis admissions. Given the tendency of these valved conduits to constrict over time, with consequent stenosis and regurgitation, they theoretically provide a rich opportunity for the seeding of bacteria. It is therefore worth noting that the 5 patients with conduit endocarditis represent less than 1% of all conduits placed during this 21-year period at the institution. Nevertheless, given the consequences of infection, all efforts at prevention should be a priority.

Table 3. Reoperations Among the Study Cohort

Pt	Endocarditis Operation	Reoperative Procedure
1	Ventricular septal defect closure	RV-PA conduit replacement
2	Mitral valve replacement	Mitral valve replacement
3	Aortic root replacement and mitral valve repair	Aortic root replacement and mitral valve repair
4	Ross operation	RV-PA conduit replacement
5	Mitral and aortic valve repair	Ross procedure and subvalvar repair of aortic stenosis
6	Ross operation and mitral valve replacement	RV-PA conduit replacement
7	RV-PA conduit replacement	Mitral valve replacement
8	Mitral valve replacement	Mitral valve replacement
9	Aortic valve replacement	Left ventricular outflow tract aneurysm
10	Mitral valve repair	Mitral valve replacement

PA = pulmonary artery; RV = right ventricle.

The surgical mortality rate of 15% is consistent with outcomes from the adult population [15]. Although the small sample size does not permit statistical predictions of risk, two trends are notable. All deaths in the series occurred in infants, 60% of whom were premature. The vulnerability of this special population has been observed by others as well [16]. In addition, 75% of patients with fungal endocarditis did not survive. These patients are clearly at particularly high risk.

The study found a remarkably high reoperation rate among patients who required surgical treatment of endocarditis. Most reoperations occurred in patients who underwent prosthetic valve replacement and required a larger prosthesis secondary to somatic growth. Although understandable, this fact highlights an important consequence of surgical therapy for endocarditis that must be considered when counseling patients and families.

Surgical treatment of IE is effective at eradicating disease. Patients who are younger than 1 year and those with fungal organisms are at high risk for death and require heightened attention and proper counseling. The reoperative rate necessitates that surgical intervention be reserved for medically refractory patients and deserves careful consideration in the risk-benefit analysis.

References

1. Coward K, Tucker N, Darville T. Infective endocarditis in Arkansan children from 1990 through 2002. Pediatr Infect Dis J 2003;22:1048–52.
2. Schollin J, Bjarke B, Wesstrom G. Infective endocarditis in Swedish children. Incidence, etiology, underlying factors, and port of entry of infection. Acta Paediatr Scand 1986;75:993–8.
3. Karaci AR, Aydemir NA, Harmandar B, et al. Surgical treatment of infective valve endocarditis in children with congenital heart disease. J Card Surg 2012;27:93–8.
4. Day MD, Gauvreau K, Shulman S, Newburger JW. Characteristics of children hospitalized with infective endocarditis. Circulation 2009;119:865–70.
5. Martin JM, Neches WH, Wald ER. Infective endocarditis: 35 years of experience at a children's hospital. Clinical infectious diseases: an official publication of the Infectious Diseases Society of America. Clin Infect Dis 1997;24:669–75.
6. Tansel T, Onursal E, Eker R, Ertugrul T, Dayioglu E. Results of surgical treatment for infective endocarditis in children. Cardiol Young 2005;15:621–6.
7. Millar BC, Jugo J, Moore JE. Fungal endocarditis in neonates and children. Pediatr Cardiol 2005;26:517–36.
8. Tissieres P, Jaeggi ET, Beghetti M, Gervaix A. Increase of fungal endocarditis in children. Infection 2005;33:267–72.
9. Hickey EJ, Jung G, Manlhiot C, et al. Infective endocarditis in children: Native valve preservation is frequently possible despite advanced clinical disease. Eur J Cardiothorac Surg 2009;35:130–5.
10. Fenoglio JJ Jr, McAllister HA Jr, DeCastro CM, Davia JE, Cheitlin MD. Congenital bicuspid aortic valve after age 20. Am J Cardiol 1977;39:164–9.
11. Delmo Walter EM, Musci M, Nagdyman N, Hübler M, Berger F, Hetzer R. Mitral valve repair for infective endocarditis in children. Ann Thorac Surg 2007;84:2059–65.
12. Pettersson G, Tingleff J, Joyce FS. Treatment of aortic valve endocarditis with the Ross operation. Eur J Cardiothorac Surg 1998;13:678–84.
13. Prat A, Saez de Ibarra JI, Vincentelli A, et al. Ross operation for active culture-positive aortic valve endocarditis with extensive paravalvular involvement. Ann Thorac Surg 2001;72:1492–6.
14. Joyce F, Tingleff J, Pettersson G. The Ross operation: Results of early experience including treatment for endocarditis. Eur J Cardiothorac Surg 1995;9:384–92.
15. Mylonakis E, Calderwood SB. Infective endocarditis in adults. N Engl J Med 2001;345:1318–30.
16. Yoshinaga M, Niwa K, Niwa A, et al. Risk Factors for in-hospital mortality during infective endocarditis in patients with congenital heart disease. Am J Cardiol 2008;101:114–8.

DISCUSSION

DR LAUREN KANE (San Antonio, TX): I want to thank the Society for allowing me to discuss this paper, Dr Austin, and Dr Cerfolio. Thank you, Dr Russell, for providing me with the manuscript well in advance. I want to congratulate you on an excellent review of an important topic in our pediatric population. I do have a couple of questions for you.

The bicuspid aortic valve is a known risk factor for developing endocarditis. It is, arguably, the second most common reason for children and infants to get endocarditis. First, why was it that you chose to consider this normal cardiac anatomy? Second, how would it have changed your data set if you had grouped it with congenital heart disease?

DR RUSSELL: I was particularly interested in those with the more severe congenital heart defects, those with large shunts, and those who had been previously palliated who contracted endocarditis. Because of the large number of patients with bicuspid aortic valves, I thought that it would give a clearer picture of the rate of endocarditis in our routine congenital heart disease population by placing them in the normal group. Had we put them in the congenital heart surgery group, we probably would have seen a 90% incidence within the congenital heart disease group, which is what some others have published. So it just depends on how you want to define it. But I thought that it made for a somewhat cleaner picture of the patients that we deal with on a day-in and day-out basis in the congenital heart disease world, who gets endocarditis and who doesn't.

DR ANASTASIOS POLIMENAKOS (Danville, PA): I really enjoyed your talk. I just want to ask you a question regarding the bioprosthetic or mechanical valve prostheses that you mentioned for endocarditis. What is the peak hazard period after replacement that you observe these endocarditis cases?

DR RUSSELL: I don't have the data in the presentation here. The average time was roughly 3 years post-op for those patients who did develop endocarditis. It was a small number of patients. So those data need to be observed with some caution; again, because of the few patients who actually did have a prosthetic valve who then contracted endocarditis. But, again, of those patients that did have one, it was around the 3-year time mark postoperatively; none were in the acute period, within 30 days of the operation.

DR CONSTANTINE MAVROUDIS (Orlando, FL): That was a very nice review of a complicated group of patients.

Complicated because the indications for operation can vary, especially with fungal endocarditis, which is a virulent organism. You showed that clearly there were some deaths in premature infants, who probably were infected due to a central venous catheter or other iatrogenic causes.

I wonder whether you have and can reevaluate the data and see which patients actually died without surgical therapy. This obviously is a matter of patient selection. Last-ditch efforts for survival, despite high risk, impacts on mortality. In short, patient selection can result in low or high mortality depending on the severity of patients that one elects to offer an operation. So I wonder whether you have any of those data that might shine more light on this topic. If not, it might be a reasonable undertaking to find out just how many patients were not treated surgically and who had similar findings. It might actually add to your conclusion in a more comprehensive way.

DR RUSSELL: Thank you for the comments. I agree with you, and that is what other authors have noted, that actually having the denominator is a challenge for any of these surgical reviews. Fungal endocarditis is clearly a bad actor, and I agree completely with you.

How these data are interpreted is going to be up to each surgeon, but I think what the data do give us is some information to counsel not only the families but also the referring physicians and neonatologists, et cetera, just how serious a disease this is that you are or are not willing to undertake in taking a child like that to the operating room.