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Original Articles

Twelve Years of Experience in the Treatment of Paediatric Infective Endocarditis

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Abstract ***Objective:*** The aim of this study was to review our 12 years of experience with the diagnosis and treatment of paediatric infective endocarditis (IE). ***Methods:*** Patients hospitalised between March 1999 and December 2011 were enrolled, and clinical data were retrospectively analysed. ***Results:*** Of the total 93 patients, 83 had underlying diseases and/or predisposing factors. Pathogenic microorganisms were detected on blood culture in 61 patients (65.6%). The positive rates of patients hospitalised between 1999 and 2007, and between 2008 and 2011, were 49.1% and 89.5%, respectively. Intracardiac vegetations were found in 82 patients. A total of 16 patients experienced embolisms, and 3 patients experienced intracranial bleeding. Heart failure occurred in 24 patients. Acute renal insufficiency occurred in 6 patients. Aortic pseudoaneurysm occurred in 2 patients. The duration of antibiotics ranged from 28 to 130 days. Surgery was performed in 58 patients after a mean of 21.88±12.4 days of antibiotic therapy. The mortalities were 44% and 3.4%, respectively, in the patients who received antibiotic therapy only and received both antibiotic and surgical therapy. ***Conclusions:*** The congenital heart defects and postoperative residual anatomical abnormalities are important factors that leave children susceptible to IE. The patients colonised with *Staphylococcus aureus* showed a tendency for embolism formation and death.

Key words Congenital heart defects; Infective endocarditis; Paediatrics; Pathogenic bacteria culture

Introduction

Infective endocarditis (IE) is one of the most serious cardiovascular diseases seen in children. With the recent decrease in the incidence of rheumatic heart disease, the percentage of IE attributable to surgery or cardiac catheterisation in children with congenital heart defects (CHDs) has greatly increased.[1,2] Because the incidence of antibiotic resistance has increased in pathogenic bacteria such as streptococci and staphylococci, the clinical course of IE and its treatment strategy have changed markedly. This paper aims to review our 12 years of experience in the diagnosis and treatment of paediatric IE.

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Methods

A total of 93 paediatric patients were enrolled in this study. All were hospitalised between March 1999 and December 2011 at Shanghai Children's Medical Center; the number enrolled comprised 0.76 per thousand total hospitalised patients during that time period. Fifty-six patients were male and 37 were female. The age of IE onset

ranged from 1 month to 17 years (mean, 7.31±4.47 years). All cases were consistent with the "Recommendation for diagnostic criteria for infectious endocarditis in children."[3] published in 2010 by The Subspecialty Group of Cardiology, Society of Pediatrics, Chinese Medical Association, and editorial board of the *Chinese Journal of Pediatrics*. According to the criteria, IE was diagnosed if one of the following clinical manifestations was observed:

1. Both primary clinical parameters: (i) repeated positive cultures showing the same species of bacteria and (ii) cardiac ultrasound indicating endocardial involvement, including intracardiac vegetations, valve perforation, or intracardiac abscess.
2. One of the above-described primary clinical parameters and 3 of the 6 secondary parameters: (i) patients with predisposing conditions including underlying cardiac disease, interventional treatment or surgery for cardiac defect, or long-term intravenous access; (ii) prolonged fever, >38°C accompanied by anaemia; (iii) aggravation of the original heart murmur or emergence of a new heart murmur or the appearance of cardiac dysfunction; (iv) important vascular signs, including arterial embolisms, infected aneurysms, ecchymosis, splenomegaly, intracranial haemorrhage, bleeding of the conjunctiva, or Janeway spots; (v) immunological features such as glomerulonephritis, Osler junction, Roth spots, or a positive rheumatoid factor test result; or (vi) positive microbiological culture but not meeting the primary clinical parameter requirements.
3. Endocardial involvement evidence and 2 of the 6 secondary parameters described above.
4. Five of the 6 secondary parameters described above.
5. Pathological examination confirming the presence of microorganisms or features of active endocarditis in a resected neoplasm or affected cardiac tissue obtained on an endomyocardial biopsy.

Clinical data were retrospectively analysed; these data consisted of underlying diseases, predisposing factors, results of cultures for microbial pathogens, presence of intracardiac neoplasms, the detection methods involved, treatment regimens, and patient outcomes.

Statistical analysis was performed using Student's *t*-test in all matched groups. All results were expressed as means ± standard error. A p value of less than 0.05 was considered significant.

Results

Underlying Diseases and Predisposing Factors

Of the 93 total patients, 83 had underlying cardiac diseases and/or factors predisposing to IE. In all, 80 patients had CHDs (Table 1), 2 had aplastic anaemia, and 1 had long-term intravenous access. Of the 80 CHD patients, 36 had a history of cardiac surgery or cardiac interventional therapy. Postoperative infections caused by artificial surgical materials or prosthetic valves occurred in 10 patients, and postoperative residual shunt and/or obstruction developed in 19 patients. The onset of IE occurred within 1 month of cardiac intervention in 9 patients, between 1 month and 1 year in 11 patients, and after 1 year in the other 16 patients.

Pathogenic Bacteria Culture

Pathogenic microorganisms were detected in 61 blood cultures (Table 2). The positive-culture rate was 65.6%. It was noted that the positive rate of blood culture in the patients admitted after 2008 increased obviously, likely owing to the increased awareness of diagnostic standards,

Table 1 Concomitant congenital heart defects

Defect	Number	Rate (%)
VSD	29	36.3
PDA	9	11.3
TOF	9	11.3
AS/SAS/COA	8	10.0
PA	5	6.3
DCRV	4	5.0
DORV	3	3.8
AVSD	3	3.8
D-TGA	2	2.5
MV lesion	5	6.3
TV lesion	1	1.3
L-TGA/VSD/PS	1	1.3
SV	1	1.3
Total	80	100

VSD: ventricular septal defect; PDA: patent ductus arteriosus; TOF: tetralogy of Fallot; AS: aortic stenosis; SAS: supravalvular aortic stenosis; COA: coarctation of the aorta; PA: pulmonary atresia; DCRV: double-chambered right ventricle; DORV: double outlet right ventricle; AVSD: atrial ventricular septal defect; D-TGA: complete transposition of the great arteries; MV: mitral valve; TV: tricuspid valve; L-TGA: corrected transposition of the great arteries; PS: pulmonary stenosis; SV: single ventricle

more attention to susceptible populations, the strict application of indications for antibiotic treatment, improved blood culture methods, and more importantly, the replacement of the blood culture system. Patients hospitalised between 1999 and 2007 had a positive-culture rate of 49.1% (27 of 55 patients), while those hospitalised between 2008 and 2011 had a positive-culture rate of 89.5% (34 of 38 patients). The difference was statistically significant ($p<0.001$). The most common microorganisms were *Streptococcus* and *Staphylococcus*. Fungal infection was found in 2 patients. One was infected with *Candida albicans*, and the other with *Candida guilliermondii.*

Fifty-four patients consented to operative treatment for the removal of intracardiac vegetations; all excised vegetations had negative cultures, with the exception of 2 that grew *Streptococcus viridans*. To increase the bacterial detection rate in the excised vegetations, polymerase chain reaction (PCR), which was first used to detect microorganisms in 2006, was performed for 12 samples, of which 10 were positive and the other 2 were negative for bacterial infection, consistent with the results observed on blood cultures.

Intracardiac Vegetations

Intracardiac vegetations were detected in 82 patients; 73 of the vegetations were detected on cardiac ultrasound examination (2DE), and 9 were detected on computed tomography (CT)/magnetic resonance imaging or surgical exploration. The overall incidence of vegetations was 88.2%. All lesions diagnosed by 2DE or CT were confirmed at surgery, which were considered the gold standard of the diagnosis. The sensitivity of 2DE in detecting intracardiac vegetations in this study was 85.7%, with a specificity of 100%. The left heart housed vegetations in 28 patients, and 45 patients had right-sided vegetations. Nine patients had vegetations present in both sides of the heart (Table 3).

Table 2 Pathogenic bacteria found on blood culture

Pathogenic bacteria	Number	Rate (%)
Streptococcus		48.3
Streptococcus viridans	26	
Streptococcus pneumoniae	2	
Streptococcus (group D)	1	
Staphylococcus		36.7
Staphylococcus aureus	12	
Coagulase-negative staphylococci	11	
Acinetobacter baumannii	2	3.3
Haemolytic Pasteurella	1	1.7
Pseudomonas aeruginosa	1	1.7
Onion Kpa Holder bacteria	1	1.7
Stenotrophomonas maltophilia	1	1.7
Gemella haemolysans	1	1.7
Fungus	2	3.3
Total	**61**	**100**

Complications

Embolism and Intracranial Bleeding

Embolism occurred in 16 patients: cerebral emboli (6 patients), pulmonary artery emboli (7 patients), and systemic arterial emboli (3 patients). Intracranial bleeding occurred in 3 additional patients. Of these 19 patients, 13 had positive blood cultures: *Staphylococcus* in 6 patients, *Streptococcus viridans* in 5, *Stenotrophomonas maltophilia* in 1, and *Candida albicans* in 1.

Table 3 Vegetation location

Location	Number
Left heart	
AV	15
MV	11
LA	1
MV + LA	1
Right heart	
TV	13
PV/RVOT	19
TV + PA	2
RV	2
VSD/RVOT patch (pericardium)	6
RVOT conduit (bovine jugular vein)	2
Blalock-Taussig shunt conduit (Gore-Tex)	1
Bilateral heart	
AV + PV	4
AV + TV	1
MV + TV	2
MV + PA	1
LV + RV	1

AV: aortic valve; MV: mitral valve; LA: left atrium; TV: tricuspid valve; PV: pulmonary valve; RVOT: right ventricular outflow tract; PA: pulmonary artery; RV: right ventricle; VSD: ventricular septal defect; LV: left ventricle

Heart Failure

Heart failure occurred in 24 patients; it was caused by severe aortic regurgitation in 7 patients, mitral valve regurgitation in 6, tricuspid valve regurgitation in 5, postoperative low cardiac output in 5, and aortic arch involvement in 1 patient.

Renal Dysfunction

Acute renal insufficiency occurred in 6 patients. In some patients, azotemia and renal tubular dysfunction occurred, abdominal ultrasonography also showed obvious bilateral kidney swelling. The nephrologists considered this drug-induced allergic inflammation and suggested the use of methylprednisolone. The results obtained were quite good, and the renal function of all patients recovered to normal.

Aortic Pseudoaneurysm

Aortic pseudoaneurysm was seen in 2 patients. One had a persistent fever 3 months after surgery to repair multiple congenital cardiac defects; local aneurysmal dilation of the aortic arch was seen on CT. Another patient was found to have stenosis of a bicuspid aortic valve and an ascending aortic pseudoaneurysm. The diagnoses of the pseudoaneurysm in these patients were confirmed by surgeries and were not related to the primary congenital heart disease.

Treatment

Antibiotic Treatment

Antibiotics were used in all 93 patients. The duration of therapy ranged from 28 to 130 days (mean, 49.29±18.85 days). Penicillin, alone was used in 2 early patients, and combined antibiotic therapy was administered in the remaining 91 cases. Among the 91 patients receiving combined therapy, 62 received 2 types of antibiotics, and 29 received 3 or more types of antibiotics.

Vancomycin was used more frequently beginning in 2005: since the beginning of that year, it was used in 57.8% of patients (37 of 64) compared with 21.4% (6 of 28 patients) before 2005 (p=0.001). Aminoglycoside use declined over the same time period; this medication class was used in 25% of patients (16 of 64) since 2005 and 53.6% (15 of 28) before 2005 (p=0.008). The use of other antibiotics showed no obvious change in frequency.

Surgical Intervention

Surgical interventions were recommended for patients with (1) mitral or aortic valve damage with severe reflux or heart failure caused by excrescence blockage; (2) fever and positive blood cultures persisting longer than 7-10 days, despite appropriate antibiotic therapy, and the extracardiac causes excluded; (3) valvular perforation or breakage, paravalvular abscess or fistula formation, local infection dissemination caused by excrescence enlargement; (4) large or unstable vegetations, especially those located in the left heart valve; (5) infection with fungi or multiple drug-resistant microorganisms; (6) underlying cardiac defect or postoperative residual constrictive abnormality requiring surgical correction.

In this group of patients, fifty-eight patients (60.2%) received surgical intervention after a mean of 21.6±11.8 days of antibiotic therapy. Of these, 12 underwent early operation within 10 days (mean, 5.67±3.4 days) of starting antibiotic therapy, including 11 emergency operations for life-threatening clinical manifestations. Five patients had severe regurgitation caused by left-sided heart valve damage, 4 had emergent emboli, 1 had right-ventricular outflow tract obstruction caused by a large vegetation, and 1 had severe postoperative right-ventricular outflow tract residual obstruction, also caused by a large vegetation. Another 46 patients underwent elective surgery after a mean of 25.74±9.5 days of antibiotic treatment. Surgery was performed when these patients were clinically stable, as evidenced by a normal body temperature, negative blood cultures, and normal C-reactive protein (CRP) and erythrocyte sedimentation rate results.

The mortality in the early-operated patients was 8% (1 of 12), and the average hospitalisation time was 43.25±12.4 days. The mortality in electively operated patients was 2.1% (1 of 46), which was not statistically different from early-operated patients (p=0.374), but the mean hospital stay was 58.88±22.36 days, much longer than early-operated patients (p=0.025).

At the time of surgery, intracardiac vegetations were carefully removed and accompanying cardiac defects were repaired. Eleven patients required valve replacement because of serious valvular damage: the aortic valve was replaced in 7 patients, the mitral valve in 3, and the tricuspid valve in 1.

Outcomes

Complete cure was achieved in 70 patients (75.3%). Five patients (5.4%) showed improvement and were transferred to a local hospital for further antibiotic treatment. Five patients (5.4%) requested discharge for various personal reasons. Thirteen patients (14.0%) died; of these, 11 had

received antibiotic therapy only, (11 of 25 with this regimen) and 2 had received both antibiotic and surgical therapies (2 of 58 with this regimen). The mortality in these treatment groups was 39.8% and 3.6%, respectively ($p<0.001$). The proportion of patients treated with antibiotics alone was indeed high, but most of the patients (10 cases) were admitted before 2008, and only 3 patients were admitted after that. The specific causes of patient death are listed in Table 4.

Discussion

Unlike adult patients, the majority of paediatric IE patients have underlying cardiac diseases-in particular, CHDs. In this series, 86% of patients had CHDs; the majority of the conditions were ventricular septal defects, patent ductus arteriosus, and tetralogy of Fallot, consistent with the rates reported in the literature.[1,2] In recent years, along with improvements in surgical techniques there has been an increasing variety of implantable artificial materials; many paediatric patients with complex CHDs have been able to be surgically treated and the postoperative survival time has been extended. Meanwhile, patients with postoperative residual abnormal anatomic structures remain at high risk for IE,[1,4,5] and this threat might last throughout their lifetime. Approximately 50% of paediatric IE patients that have CHDs have a history of cardiac reparative surgery.[5,6] In this series, 45% of patients had undergone previous surgery; 52.8% of these had obvious postoperative residual shunts or obstructions. These postoperative residual defects should be corrected as soon as possible in order to reduce the risk of IE. For those patients complicated by a mild-to-moderate degree of postoperative valvular regurgitation, who do not have an indication for immediate re-operation, the risk of IE and preventive measures should be explained. In addition, non-specialised medical institutions should be informed as to appropriate preventive measures for these high-risk patients, with the aim of effectively reducing the incidence of IE.[7]

Approximately 10% of paediatric IE patients do not have structural cardiac abnormalities. In these patients, the aortic or mitral valves are likely to be involved, and the most common pathogen is *Staphylococcus aureus*.[1,8] In this series, 13 paediatric IE patients (14.1%) had no cardiac structural defect; the aortic or mitral valve was infected in 10 patients. Blood cultures were positive in 8 patients, of which 5 cultures were positive for *Staphylococcus aureus*; these rates are similar to those seen in the published literature.

Some authors report positive blood culture rates from 60% to 90%.[9-11] In this series, the overall positive blood culture rate was 65.6%, gradually increasing over the years of the study. This rise in positive rates may be due to increasing awareness of diagnostic standards, more attention to susceptible populations, strict application of

Table 4 Pathogenic bacteria and cause of death

Underlying diseases	Blood culture	Surgery	Cause of death
PDA/SAS	*Staphylococcus aureus*	No	Refractory heart failure
TOF, S/P, residual defect	*Staphylococcus aureus*	No	Ventricular tachycardia
No defect or disease	*Staphylococcus aureus*	No	Mesenteric embolism
DORV	*Streptococcus viridians*	No	Cardiogenic shock
VSD	*Streptococcus viridians*	Yes	Cerebral embolism
D-TGA/IVS, S/P	*Candida guilliermondii*	No	Uncontrolled infection
TOF	*Candida albicans*	No	Cardiogenic shock
PDA/MR, S/P, residual defect	Negative	No	Intracranial haemorrhage
VSD, S/P	Negative	No	Acute pulmonary embolism
PA/VSD, S/P	Negative	No	Uncontrolled infection
VSD/MR	Negative	Yes	Ventricular tachycardia
Aplastic anaemia	Negative	No	Cerebral embolism
Aplastic aneamia	Negative	No	Cardiogenic shock

PDA: patent ductus arteriosus; SAS: supravalvular aortic stenosis; TOF: tetralogy of Fallot; S/P: post-operation; DORV: double outlet right ventricle; VSD: ventricular septal defect; D-TGA: complete transposition of the great arteries; IVS intact ventricular septum; MR: mitral valve regurgitation; PA: pulmonary atresia

indications for antibiotic treatment, and improved blood culture methods. In susceptible populations, if a fever of unknown origin lasts 3 to 7 days and serum CRP is increased, double blood samples from different sites should be drawn for culture before antibiotic treatment is started. If no bacterial growth is found after 48 to 72 hours, blood sampling should be performed at different sites for repeat culture. The choice of antibiotic should be made according to the clinical severity of the patient's disease. If patients are in serious condition or vegetations have been detected, especially when vegetation movement is obvious, antibiotic treatment should begin immediately after sampling for blood cultures. In susceptible patients who do not meet the above criteria, antibiotic treatment may be delayed until positive blood cultures or the results of drug-sensitivity tests are confirmed. If susceptible patients are already using antibiotics and blood culture has not yet been performed, intravenous antibiotics may be stopped for 48 to 72 hours before sampling, if the clinical condition permits, in order to increase the chance of a positive culture. Further treatment principles are the same as those mentioned above. PCR testing of vegetations or blood is a new option for detecting pathogenic bacteria.[12-14] Some authors have doubted that PCR has higher specificity than blood culture and the clinical significance of this testing modality needs to be studied further for clarity.

Gram-positive cocci, especially *Streptococcus viridans* and *Staphylococcus aureus*, are the main pathogens seen in paediatric IE patients.[5,15,16] In recent years, some authors have reported that *Staphylococcus aureus* infections exceed *Streptococcus viridians* infections in certain geographic areas.[16,17] In this series, *Streptococcus* was detected in 29 of 61 (47.5%) culture-positive patients; *Staphylococcus aureus* was found in 23 (37.7%). These 2 pathogens were found in almost 85.2% of culture-positive patients, whereas Gram-negative bacilli were found in only 10.7%. These results are similar to those reported in the literature and to the results of our previous study in 2001.[18]

In the last 10 years, most streptococcal strains and almost all *Staphylococcus aureus* bacteria have developed various degrees of resistance to penicillin; vancomycin has been the first treatment choice for these resistant strains.[19,20] In this series, vancomycin was used frequently since the beginning of 2005. Skin rash occurred in some patients taking vancomycin, and 2 patients developed temporary renal impairment manifested by recurrent vomiting, a significant decrease in the 24-hour creatinine clearance rate, and an enlargement of kidney volume. After stopping the medication and administering methylprednisolone, all patients recovered. Since 2008, 6 patients taking vancomycin for staphylococcus or streptococcus infections developed intractable fever. After linezolid was chosen as the primary medication for resistant patients at our institution, improved clinical effects were achieved and no serious side effects occurred.

Intracardiac vegetations are an important diagnostic criteria for IE, and 2DE is the most commonly used method to detect these vegetations. 2DE is also a valuable method to investigate signs of local infectious foci progression, such as paravalvular abscess, pseudoaneurysm, fistula, and neoplasm enlargement.[21] The method also has the advantage of being noninvasive and well repeatable. In this series, 72 patients (78.3%) had vegetations revealed by 2DE; the sensitivity and specificity of 2DE to detect vegetations reached 85.7% and 100%, respectively. To further improve the detection rate, the different hemodynamic features and usual vegetation sites of various CHDs should be well understood by cardiologists and ultrasound technicians. These personnel should be informed of suspected cases of IE in a timely fashion, and repeat 2DE examination should be performed in order to avoid misdiagnosis.

Distal vascular embolism, induced by intracardiac vegetation shedding, was a common cause of death. Shedding occurred in 20% to 50% of all patients with vegetations.[19] Patients infected with *Staphylococcus aureus* had a higher incidence of embolism than those with other bacterial infections.[22] The risk of embolism decreased significantly after antibiotic treatment, in particular, after 2 weeks of consistent antibiotic use.[19] A total of 19 patients in our series experienced embolic events, of which 6 had cerebral emboli; the incidence and the implicated bacterial strains were consistent with other reports.[5,6] The most effective measure to reduce the risk of embolic events is antibiotic treatment, initiated as early as possible. Surgery to remove vegetations and prevent embolic events is another option, but the previous embolic event history, the vegetation's size and its swing degree, the duration of antibiotic therapy, and any other complications should be considered to entirely understand the benefits and risks of this treatment.

Heart failure is another common complication of acute IE. It can progress to severe heart failure if valvular reflux is present; reflux is usually caused by valvular perforation or chordae rupture. Factors influencing the degree of heart failure severity, from highest impact to lowest, are aortic valve regurgitation, mitral valve regurgitation, and tricuspid valve regurgitation.[23] If patients receive valve replacement for refractory heart failure in the acute phase, the incidence

of re-infection is between 2% and 3%.[24,25] The risk of postoperative re-infection in these severely ill patients is much lower than that in patients who received antibiotics treatment only.[23]

It is reported that the in-hospital mortality of IE patients ranges from 9.6% to 26%, and the 1-year mortality ranges from 20.6% to 31%.[26] Acute heart failure, cerebral embolism, and refractory infection are the 3 main causes of death. Ohara et al[27] reported, in a series of 348 native valve endocarditis patients, that the mortalities in patients treated with antibiotics alone or with both antibiotic administration and surgical interference were 26% and 4% respectively. Yoshinaga reported surgical intervention emerged as an independent predictive factor for lower in-hospital mortality in IE patients with congenital heart disease. Our results were similar: mortality in our series was much higher in patients receiving only medical treatment than in those receiving a combination of medical and surgical treatment (44% vs. 3.4%).

According to the guidelines published by the European Society of Cardiology, patients with IE can be divided into categories depending on the time frame of surgery: emergency, within 24 hours; sub-emergency, within a few days; and elective, after 1 to 2 weeks of treatment.[19] Choosing a suitable surgical time is very important for reducing postoperative mortality. Traditionally, surgery was performed after 4 to 6 weeks of antibiotic treatment in order to control infection, and early operation was thought to increase postoperative mortality, prolong postoperative mechanical ventilation, and extend the duration of the intensive care unit stay. In recent years, however, reports have tended to frequently describe early operations; this treatment option is being considered a preventive measure as it dislodges bacterial emboli and prevents progressive damage to the affected valves and may have the advantage of improving short- and long-term prognoses.[28,29] In this series, although the mortality was not different between 12 early surgery patients and 46 elective surgery patients, the duration of hospital stay was significantly decreased in patients with early operations. In some circumstances, emergency surgery might save patients' lives. If a patient is found to have a vegetation with an obviously large swing, especially with blood cultures positive for *Staphylococcus aureus* or fungus, emergency surgery should be performed to remove the vegetation. The pendulous vegetations induced by such pathogenic microbes are friable and easily dislodged. In addition, if the aortic or mitral valve is affected and refractory pulmonary edema or if cardiogenic shock exists, emergency surgery should be undertaken as early as possible because any delay might greatly increase postoperative risk.[19]

On the basis of the results of this study, we shall further accumulate new cases admitted in recent years and collect parameters more in detail so that we can compare the differences between the earlier and later time periods as well as risk factors of mortality and morbidity using single factor and multivariate analysis.

Conclusions

CHDs and postoperative residual anatomical abnormalities are important risk factors in paediatric IE. *Streptococcus viridans* and *Staphylococcus aureus* are the most important pathogenic bacteria. Patients infected with *Staphylococcus aureus* have a high risk of embolism and death. Acute heart failure, cerebral embolism, and refractory infection are the main causes of death in paediatric IE patients. Sensitive blood culture technique and timely operative therapy can effectively reduce hospital mortality and improve patient outcomes.

Declaration of Interest

There are no conflicts of interest to declare.

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