CONGENITAL HEART DISEASE

ORIGINAL ARTICLES

Surgical Treatment of Infective Valve Endocarditis in Children with Congenital Heart Disease

Ali Riza Karaci, M.D.,* Numan Ali Aydemir, M.D.,* Bugra Harmandar, M.D.,* Ahmet Sasmazel, M.D.,* Turkay Saritas, M.D.,† Zeliha Tuncel, M.D.,‡ and Ibrahim Yekeler, M.D.*

**Department of Pediatric Cardiac Surgery; †Department of Pediatric Cardiology; ‡Department of Anesthesiology and Reanimation, Dr. Siyami Ersek Thoracic and Cardiovascular Training and Research Hospital, Istanbul, Turkey*

ABSTRACT ***Objective:*** **This study assesses surgical procedures, operative outcome, and early and intermediate-term results of infective valve endocarditis in children with congenital heart disease.** ***Methods:*** **Seven consecutive children (five females, two males; mean age, 10.8 years) who underwent surgery for infective valve endocarditis between 2006 and 2010 were included in the study. The aortic and mitral valves were affected in two and tricuspid in five patients. Indications for operation included cardiac failure due to atrioventricular septal rupture, severe tricuspid valve insufficiency, and septic embolization in one, moderate valvular dysfunction with vegetations in three (two tricuspid, one mitral), and severe valvular dysfunction with vegetations in the other three patients (two tricuspid, one mitral). The pathological microorganism was identified in five patients. Tricuspid valve repair was performed with ventricular septal defect (VSD) closure in five patients. Two patients required mitral valve repair including one with additional aortic valve replacement.** ***Results:*** **There were no operative deaths. Actuarial freedom from recurrent infection at one and three years was 100%. Early echocardiographic follow-up showed four patients to have mild atrioventricular valve regurgitation (three tricuspid and one mitral) and three had no valvular regurgitation. No leakage from the VSD closure or any valvular stenosis was detected postoperatively.** ***Conclusions:*** **Mitral and tricuspid valve repairs can be performed with low morbidity/mortality rates and satisfactory intermediate-term results in children with infective valve endocarditis.** doi: 10.1111/j.1540-8191.2011.01339.x *(J Card Surg 2012;27:93-98)*

Infective valve endocarditis, although less common in childhood, appears to be increasing.[1-5] Children with untreated congenital cardiac defects, including bicuspid aortic valve, ventricular septal defect (VSD), patency of the ductus arteriosus, and tetralogy of Fallot, have a higher risk for developing infective endocarditis as well as children undergoing surgery due to congenital heart defects.[1-9]

Although improved outcomes have been reported over time for the treatment of infective endocarditis in children, current hospital mortality rates of 10% to 20% following medical treatment alone [2-5,8] or perioperative death rates of 0% to 50% demonstrate the severity of this condition.[5-11]

The purpose of this report is to present our surgical experience with valvular endocarditis in children with congenital heart defects.

MATERIAL AND METHODS

The Institutional Review Board approved the retrospective study and waived the need for patient consent.

Between March 2006 and June 2010, seven consecutive children with previously diagnosed congenital heart defects underwent surgical repair for infective valve endocarditis. Previously normal hearts or acquired lesions were excluded. Clinical records were reviewed for patient demographic data, operative findings, surgical techniques used, postoperative course, and follow-up. There were five females and two males with a mean age of 10.8 years (range 7.3 to 13.4 years).

Conflict of interest: The authors declared no conflicts of interest with respect to the authorship and/or publication of this article.

Funding: The authors received no financial support for the research and/or authorship of this article.

Address for correspondence: Dr. Bugra Harmandar, M.D., Dr. Siyami Ersek Gogus, Kalp ve Damar Cerrahisi Egitim ve, Arastirma Hastanesi, Kalp Cerrahisi Klinigi, 34668, Haydarpasa, Istanbul, Turkey. Fax: +902163379719; e-mail: dr.bugra@gmail.com

Follow-up

Data on patients' preoperative clinical features, operations, clinical course, pathologic, microbiologic findings, survival, and follow-up course were obtained through a detailed review of hospital medical records. Follow-up data were provided by the Department of Pediatric Cardiology and by the referring physicians. 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 2.3 years (range 0.5 to 4.3 years) with a total of 16.3 patient-years.

RESULTS

Preoperative clinical and pathological features

All seven patients had native valve endocarditis. The tricuspid valve was infected in five and the mitral valve in two patients. Patients with mitral valve infection had aortic valve involvement as well. Fever was the most common symptom in all patients, being present for a mean duration of 32.2 ± 11.2 days (range 21 to 42 days).

Congenital cardiac disease was the only predisposing factor identified in all patients. Previous diagnosis including an isolated small VSD was present in two, small VSD with congenital bicuspid aortic valve in three, and isolated congenital bicuspid aortic valve in two patients. No prior dental or any other surgical procedure was present in any patient. Except for one patient with moderate aortic stenosis, no other patient had a history of valvular insufficiency or stenosis before the onset of symptoms of infective endocarditis.

Five patients had congenital bicuspid aortic valve (three patients with tricuspid valve and two with mitral valve infection). All five patients with tricuspid valve involvement had a small VSD. Three patients had severe and two had moderate tricuspid valve insufficiency among the group of patients with tricuspid valve infection. One of the patients with mitral valve infection had moderate and the other had severe mitral valve insufficiency. Vegetations were detected in all seven patients on preoperative echocardiography. One patient with a bicuspid aortic valve and mitral infection had moderate aortic valve stenosis; however, no patient had aortic valve insufficiency. One patient with a preoperatively diagnosed small VSD and congenital bicuspid aortic valve developed atrioventricular septal rupture and leaflet perforation on the tricuspid valve. This patient had cerebral embolization and neurologic deficits as well. Despite medical treatment of cardiac failure with inotropic support and diuretics, intractable heart and renal failure led to an emergency operation. The demographic, clinical, and laboratory data of patients are presented in Table 1.

The pathological pathogens were identified in five patients (*Staphylococcus aureus* in three, *Streptococcus oralis* in one, and *Streptococcus viridans* in one). The mean duration of antibiotic treatment was 27.1 ± 8.9 days (range 19 to 36 days), preoperatively.

The most common indication for surgery was valve dysfunction (three severe and two moderate tricuspid valve insufficiencies, one severe and one moderate mitral valve insufficiency), congestive heart failure, septic embolization, and severe tricuspid valve insufficiency (one patient). All patients were diagnosed with infective endocarditis according to the revised Duke criteria with fever being the most common symptom and all patients had vegetations detected on echocardiography. The size and location of vegetations are summarized in Table 1.

Surgery and intraoperative findings

All operations were performed through a median sternotomy under cardiopulmonary bypass and moderate systemic hypothermia. Standard aortic and bicaval central cannulation was performed. Antegrade intermittent cold blood cardioplegia was used for myocardial protection. The approach was through a left atriotomy and aortotomy in two patients with mitral and aortic valve infections. A right atriotomy was performed in five patients with VSD and tricuspid valve infection. Following right or left atriotomy, the annulus, leaflets, chordae tendinae, and papillary muscles were exposed and carefully inspected to determine the extent of valvular and subvalvular damage caused by infection (Fig. 1). Our standard operative principles were the debridement of all infected tissues, cleansing of all affected areas with povidone iodine solution, reconstruction of defects, and closure of VSD using untreated fresh autologous pericardium. An attempt was made to preserve the native valve and avoid the use of prostethic materials whenever possible.

All patients underwent removal of vegetations and valve repair (five tricuspid, two mitral, and two aortic valve repair), whereas one patient required a subsequent aortic valve replacement. Five patients underwent concomitant VSD closure with fresh autologous pericardium using a continuous 6/0 polypropylene suture technique. During VSD closure, three to four pledgeted (with fresh pericardium) sutures were used to reinforce the sutures and to decrease the stress on the suture. Following the removal of vegetations and neighboring infected valve tissues, all resulting defects were repaired with fresh autologous pericardium using a continuous 7/0 polypropylene suture technique. Leaflet perforations were closed in two patients (one mitral and one tricuspid) with fresh autologous pericardium in the same manner. One of the patients who had a previously diagnosed small VSD developed atrioventricular septal rupture following infective endocarditis. This patient had a 15-mm perforation of the atrioventricular septum causing a true Gerbode defect with a left ventricle to right atrium communication. Fresh blood clots and vegetations were observed extending toward the right atrium through this perforation. The atrioventricular septal rupture was repaired using fresh autologous pericardium with 6/0 polypropylene and continuous suture technique. One patient underwent removal of

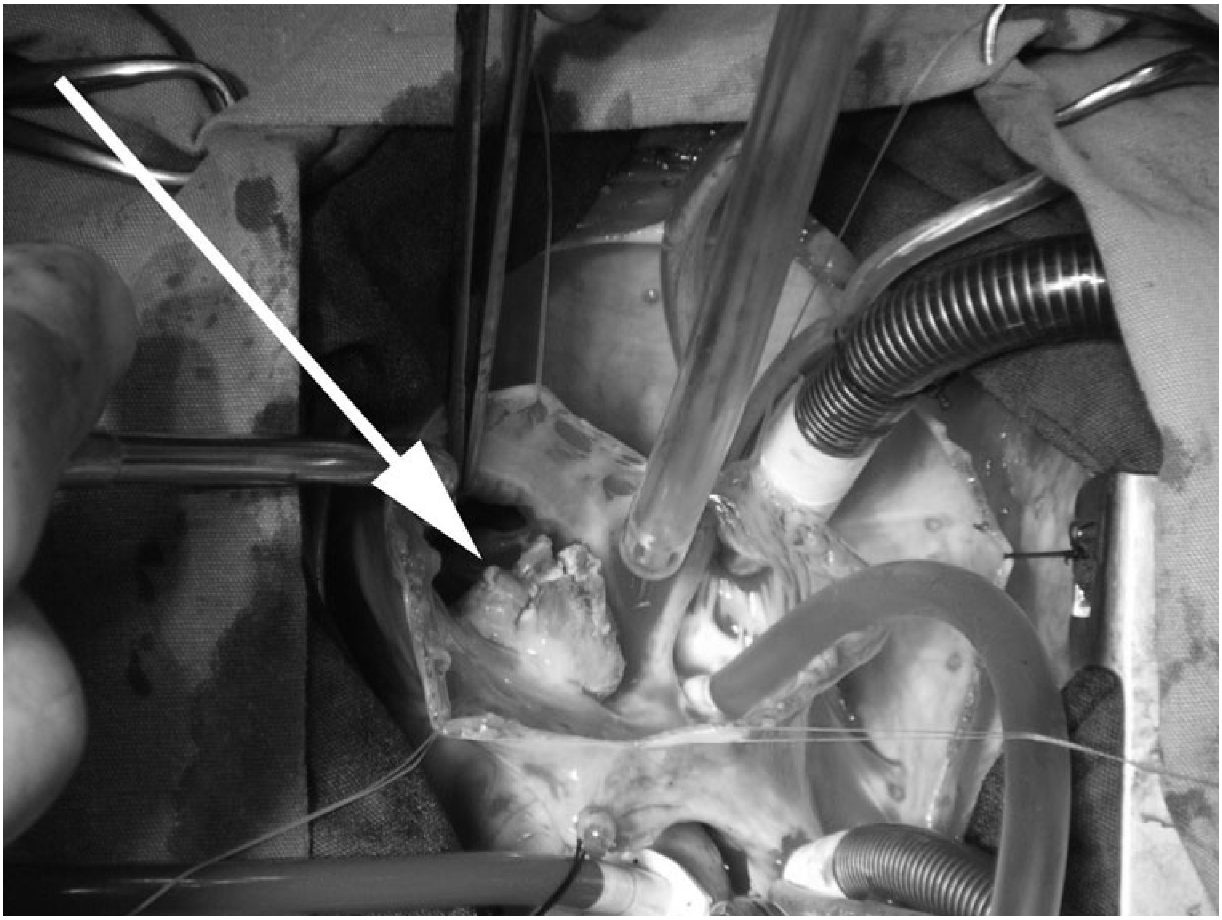

Figure 1. *Large vegetation on tricuspid valve, septal leaflet (white arrow).*

vegetations and a commissurotomy for a stenotic aortic valve. The resulting defect was repaired with fresh autologous pericardium. Intraoperative transesophageal echocardiography showed the persistence of aortic valve stenosis (45 mmHg) and severe insufficiency that eventually led to aortic valve replacement with a mechanical valve. Another patient with aortic valve infection required removal of vegetations and pericardial patching of the resulting defect. This patient had a fully competent aortic valve following the surgical procedure as shown on the intraoperative transesophageal echocardiography.

Following removal of all vegetations and closure of resulting defects, mitral valve reconstructions were performed using an anterior commissuroplasty (modified Kay–Wooler annuloplasty technique) in both patients with either moderate or severe mitral insufficiency. Tricuspid valve reconstructions included approximation of the anterior and septal leaflets at the anteroseptal commissure using pledgeted (with fresh pericardium) sutures in three patients, and plication of the posterior leaflet with extensive resection (almost 3/4 of the posterior and 1/3 of the septal leaflet) in one patient. Mean cardiopulmonary bypass and cross-clamp times were 156.5 $\pm$ 62.5 minutes (range 94 to 189 minutes) and 74.36 $\pm$ 53.2 minutes (56 to 144 minutes), respectively.

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

Mortality and morbidity

There was no operative mortality or morbidity. Mean hospital stay duration was 9.3 $\pm$ 3 days (range 6 to 14 days). No patient developed any complication. Antibiotic treatment was continued for a mean of 43.2 $\pm$ 5.9 days (range 37 to 52 days), postoperatively.

Follow-up

Intermediate-term follow-up data were complete (mean 2.3 years; range 0.5 to 4.3 years, total 16.3 patient-years). No patient was lost to follow-up. Intraoperative and early postoperative echocardiographic evaluation showed four patients to have mild atrioventricular valve regurgitation (three tricuspid and one mitral) and three had no valvular regurgitation (two tricuspid and one mitral). No valve repair resulted in valvular stenosis and no leakage from the VSD closure was detected either intraoperatively or in the early and intermediate postoperative periods. No valvular stenosis or insufficiency was present on the prosthetic aortic valve. Fever was not observed in any of

TABLE 1
Demographic Data of Patients

Patient No.	Age (years)	Sex	Previous Congenital Heart Disease	Signs or Symptoms	Physical Examination, Laboratory, and Radiology	Echocardiography	Microbial Organism
1	7.3	F	Small VSD, bicuspid aortic valve	Fever, fatigue	Tachycardia, systolic murmur, hepatomegaly, cardiomegaly, lung infiltrations, leukocytosis, high CRP and sedimentation rate	Severe tricuspid valve insufficiency, three vegetations (range 5.3 to 10.7 mm in diameter) on anterior and septal leaflets of tricuspid valve	*Staphylococcus aureus*
2	13.4	F	Bicuspid aortic valve	Fever, fatigue	Tachycardia, systolic murmur, leukocytosis, high CRP and sedimentation rate	Moderate mitral valve insufficiency, aortic valve stenosis (mean gradient 45 mmHg), vegetations on anterior leaflet of mitral and ventricular surface of bicuspid aortic valve (18×20 mm and 0.8×12 mm in diameter, respectively)	*Streptococcus oralis*
3	11.1	F	Small VSD, bicuspid aortic valve	Fever, nausea, emesis, congestive heart failure, septic emboli, convulsion, anuria	Tachycardia, hypotension, systolic murmur, hepatomegaly, peripheral edema, abdominal ascites, hyperpnoea, mental confusion, amaurosis fugax, leukocytosis, high CRP and sedimentation rate, high BUN and creatinine levels, acidosis, hypocapnia and high base excess, septic emboli and abscess formation in cranial CT	Atrioventricular septal rupture (11×28 mm in diameter with LV-RA communication—Gerbode type defect), severe tricuspid valve insufficiency, perforation on tricuspid anterior leaflet, vegetation on free wall of right atrium (31×9 mm in diameter)	*Staphylococcus aureus*
4	9.6	M	Small VSD	Fever, fatigue	Tachycardia, systolic murmur, leukocytosis, high CRP and sedimentation rate	Moderate tricuspid valve insufficiency, two vegetations (6×4 and 18×3 mm in diameter) on septal leaflet of tricuspid valve	Not identified
5	12.1	F	Small VSD, bicuspid aortic valve	Fever, fatigue	Tachycardia, systolic murmur, hepatomegaly, cardiomegaly, lung infiltrations, leukocytosis, high CRP and sedimentation rate	Severe tricuspid valve insufficiency, perforation on anterior leaflet of tricuspid valve, two vegetations (10×6 and 12×1 mm in diameter) on anterior and septal leaflets of tricuspid valve	*Staphylococcus aureus*
6	11.8	F	Bicuspid aortic valve	Fever, fatigue	Tachycardia, systolic murmur, leukocytosis, high CRP and sedimentation rate	Severe mitral valve insufficiency, perforation on mitral anterior leaflet, vegetations on anterior leaflet of mitral and bicuspid aortic valve (9×15 mm and 4×8 mm in diameter, respectively)	*Streptococcus viridans*
7	10.5	M	Small VSD	Fever, fatigue	Tachycardia, systolic murmur, leukocytosis, high CRP and sedimentation rate	Moderate tricuspid valve insufficiency, three vegetations (range 3×4 to 10×3 mm in diameter) on anterior and septal leaflet of tricuspid valve	Not identified

VSD = ventricular septal defect; CRP = C-reactive protein; BUN = blood urine nitrogen; CT = computerized tomography; LV = left ventricle; RA = right atrium, mm: millimeter.

the patients postoperatively. Repeated blood cultures were negative for microbial infection in all patients. Intermediate-term follow-up showed no recurrence of infection while mild atrioventricular valve regurgitation persisted in four patients. No late stenosis on any valve or paravalvular leakage on the replaced mechanical aortic valve was observed in intermediate-term follow-up. Actuarial freedom from recurrent infection at one and three years was 100%.

DISCUSSION

Despite reports on improved outcomes over time, infective endocarditis in infancy and childhood remains a most serious condition. Infective endocarditis is an uncommon infection and accounted for a hospitalization rate of 0.21 per 1000 pediatric admissions per year in our hospital. In the past five years, a mean of 3.4 patients were treated per year. Our incidence of infective endocarditis is similar to the previously published papers reporting an increasing incidence ranging from 0.2 to 0.9 cases per 1000 pediatric hospital admissions per year.[2,5] Patients with untreated congenital cardiovascular abnormalities are at a much higher risk for developing infective endocarditis than the general population.[1-9] Although the reported rate of infective endocarditis in patients with congenital heart disease is as low as 1%,[12] the frequency appears to be increasing according to several reports.[2,4,5]

The risk of infective endocarditis in congenital heart disease is closely related to abnormal intracardiac shunts and flow accelerations. Congenital heart defects particularly associated with high-velocity or turbulent flows, such as VSD, aortic stenosis, coarctation of the aorta, and patent ductus arteriosus, are at a much higher risk for developing infective endocarditis. Conversely, defects such as secundum atrial septal defects are not associated with infective endocarditis.[12,13]

Prior to surgical intervention for congenital heart disease, infective endocarditis is most common in patients with bicuspid aortic valves, VSDs, patent ductus arteriosus, and tetralogy of Fallot.[1-8,14] In a previously reported series of 16 children with endocarditis, 12 had cardiovascular disease with 3 having undergone a previous corrective cardiac surgery while 4 patients had no underlying cardiac disease.[1] Infective endocarditis occurring after VSD repair is reported to be mainly associated with a residual leak.[15]

Patients who are candidates for surgical intervention should be selected cautiously, since about 80% to 90% of children with infective endocarditis are expected to survive solely with conservative medical treatment. The indications for surgery in our series were valve dysfunction, congestive heart failure, septic embolization, and vegetations. Although echocardiography provides useful information on the size and other morphological features of vegetations, this is not adequate to predict the possibility of embolization.[4,16,17] Infection located outside the heart, such as on shunts, collaterals, and conduits, are difficult to demonstrate by any method. Transthoracic echocardiography was reported to have a positive finding in 59% of the patients with infective endocarditis in a previous report.[18] Transesophageal echocardiography often yields important data. Although vegetations and/or abcess formations were better demonstrated with transesophageal echocardiography, it should not be performed in patients with severe hypoxemia or toxemia.[19-22] Nevertheless, transthoracic echocardiography was successful in demonstrating the valvular vegetations in all of the seven patients presented in our report.

Our medical therapy consists of dual intravenous antibiotics for synergistic effect. Intravenous penicillin G and gentamicin, with further adjustment depending on the blood culture organism and sensitivities, are given for at least 21 fever-free days before they are stopped. The total duration of antibiotics is further adjusted for each patient according to the results of repeat blood cultures and echocardiography findings.

In our opinion, 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.

At least 40% of cases of infective endocarditis occurring in repaired congenital heart disease are now caused by staphylococcal species.[14] However, it is noteworthy that in as many as 20% of reported children with no known predisposing factors, the organism was *Staphylococcus aureus*. Similarly, three of five patients in our study group (60%), whose microorganism could be identified, had a *Staphylococcus aureus* infection. These patients were previously diagnosed with congenital heart defects but were not repaired. This emphasizes the potential threat of this organism in patients with unrepaired congenital heart defects.

The review of the current literature comparing valve replacement and repair in children with infective valve endocarditis revealed conflicting results. One study reported a high rate of valve replacement as high as 63%, due to cusp perforation, abscess formation, and chordal rupture.[1] Other studies report native valve preservation rate as high as 55% to 72%.[11,23] One recent study reports the rate of native valve preservation in children with infective valve endocarditis as high as 73% and concludes that native valve preservation was frequently possible despite advanced clinical disease.[15] Although abscess formation was not encountered in the series of our patients, existing leaflet perforations were successfully repaired in two patients (one mitral, one tricuspid) with fresh autologous pericardium and no valve replacement was required as a consequence of a leaflet perforation.

When the valve annulus is dilated, annuloplasty is our choice for the repair of an infected valve. We refrain from using a prosthetic valve or ring as much as possible in support of previous reports which advise avoiding prosthetic valves or rings in childhood.[24] We use pledgets prepared with fresh autologous pericardium for suture reinforcement. Pledgets have two distinct advantages: first, no prosthetic material is introduced into the infective operative field and second, the need for anticoagulation is obviated. Valve repair preserves viable native tissues that are more resistant to infection than prosthetic material. This approach may be considered as one of the major factors contributing to our favorable postoperative outcome.

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.[25] However, they have the problems of accelerated calcification, particularly in young children, limited durability, and availability.[26] Modern mechanical low profile bileaflet valves perform well in the aortic position, have long durability, and can be remarkably resistant to re-infection.[27] Due to the above features of mechanical valves, we used a mechanical aortic valve in one of our patients in whom an attempt to repair the aortic valve was unsuccessful.

This study is limited by the small number of subjects. In this small series, we have shown that mitral and tricuspid valve repairs are safe in children with infective endocarditis. No operative, early, or intermediate-term mortality was observed. All patients had good functional status during intermediate-term follow-up and no one had undergone mitral or tricuspid valve replacement.

REFERENCES

1. Alexiou C, Langley SM, Monro JL: Surgery for infective valve endocarditis in children. Eur J Cardiothorac Surg 1999;16:653-659.
2. Martin JM, Neches WH, Wald E: Infective endocarditis: 35 years of experience at a children's hospital. Clin Infect Dis 1997;24:669-675.
3. Tansel T, Onursal E, Eker R, et al: Results of surgical treatment for infective endocarditis in children. Cardiol Young 2005;15:621-626.
4. Awadallah SM, Rae-Ellen KW, Byrum CJ, et al: The changing pattern of infective endocarditis in childhood. Am J Cardiol 1991;68:90-94.
5. Fukushige J, Iragashi H, Ueda K: Spectrum of infective endocarditis during infancy and childhood: 20-year review. Pediatr Cardiol 1994;15:127-131.
6. Ferrieri P, Gewitz MH, Gerber MA, et al: Unique features of infective endocarditis in childhood. Pediatrics 2002;109:931-943.
7. Citak M, Rees A, Mavroudis C: Surgical management of infective endocarditis in children. Ann Thorac Surg 1992;54:755-760.
8. Nomura F, Penny DJ, Manahem S, et al: Surgical intervention for infective endocarditis in infancy and childhood. Ann Thorac Surg 1995;60:9-15.
9. Fisher MC. Changing risk factors for pediatric infective endocarditis. Curr Infect Dis Resp 2001;3:333-336.
10. Normand J, Bozio A, Etienne J, et al: Changing patterns and prognosis of infective endocarditis in childhood. Eur Heart J 1995;16:28-31.
11. Picarelli D, Leone R, Duhagon P, et al: Active infective endocarditis in infancy and childhood: Ten year review of surgical therapy. J Card Surg 1997;12:406-411.
12. De Gevigney D, Pop C, Delahaye JP: The risk of infective endocarditis after cardiac surgical and interventional procedures. Eur Heart J 1995;16:7-14.
13. Michel PL, Acar J: Native cardiac disease predisposing to infective endocarditis. Eur Heart J 1995;16:2-6.
14. Morris CD, Reller MD, Menashe VD: Thirty-year incidence of infective endocarditis after surgery for congenital heart defect. JAMA 1998;279:599-603.
15. 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;35:130-135.
16. Dillon T, Meyer RA, Korfhagen JC, et al: Management of infective endocarditis using echocardiography. J Pediatr 1980;86:552-558.
17. Humpl T, McCrindele BW, Smallhorn JF: The relative roles of transthoracic compared with transesophageal echocardiography in children with suspected endocarditis. J Am Coll Cardiol 2003;41:2068-2071.
18. Li W, Somerville J: Infective endocarditis in the grown-up congenital heart (GUCH) population. Eur Heart J 1998 Jan;19:166-173.
19. Daniel WG, Mugge A, Martin RP et al: Improvement in diagnosis of abscess associated with endocarditis by transesophageal echocardiography. N Engl J Med 1991; 324:795-800.
20. Mugge A, Daniel WG, Frank G, et al: Echocardiography in infective endocarditis: Reassessment of prognostic implications of vegetation size determined by the transthoracic and transesophageal approach. J Am Coll Cardiol 1989;14:631-638.
21. Rohmann S, Darius H, Makowski T, et al: Follow-up of vegetation by transesophageal echocardiography—prognostic implications (Abstr). Circulation 1990; (Suppl 3):P170.
22. Rohmann S, Erbel R, Mohr-Kahaly S, et al: Use of transesophageal echocardiography in diagnosis of abscess in infective endocarditis. Eur Heart J 1995;16(Suppl B): 54-62.
23. Horvath P, Hucin B, Slavik Z, et al: Operative treatment of infective endocarditis in children. Eur J Cardiothorac Surg 1989;3:26-32.
24. Delmo Walter EM, Musci M, Nagdyman N, et al: Mitral valve repair for infective endocarditis in children. Ann Thorac Surg 2007;84:2059-2065.
25. Haydock D, Barrat-Boyes B, Macedo T, et al: Aortic valve replacement for active infectious endocarditis. A comparison of freehand allograft valves with mechanical prostheses and bioprostheses. J Cardiovasc Surg 1990;103:130-139.
26. Clarke DR, Campbell DN, Hayward AR, et al: Degeneration of aortic valve allografts in young recipients. J Thorac Cardiovasc Surg 1993;105:934-942.
27. Alexiou C, Langley SM, Stafford H, et al: Surgery for active culture-positive endocarditis: Determinants of early and late outcome. Ann Thorac Surg 2000;69:1448-1454.