Thirty-Year Incidence of Infective Endocarditis After Surgery for Congenital Heart Defect

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Context.—The incidence of infective endocarditis after surgical repair of congenital heart defects is unknown.

Objective.—To determine the long-term incidence of endocarditis after repair of any of 12 congenital heart defects in childhood.


Setting.—State of Oregon.

Participants.—All Oregon residents who underwent surgical repair for 1 of 12 major congenital defects at the age of 18 years or younger from 1958 to the present.

Main Outcome Measure.—Diagnosis of infective endocarditis confirmed by hospital or autopsy records.

Results.—Follow-up data were obtained from 88% of this cohort of 3860 individuals through 1993. At 25 years after surgery, the cumulative incidence of infective endocarditis was 1.3% for tetralogy of Fallot, 2.7% for isolated ventricular septal defect, 3.5% for coarctation of the aorta, 13.3% for valvular aortic stenosis, and 2.8% for primum atrial septal defect. In the cohorts with shorter follow-up, at 20 years after surgery the cumulative incidence was 4.0% for dextrotransposition of the great arteries; at 10 years, the cumulative incidence was 1.1% for complete atrioventricular septal defect, 5.3% for pulmonary atresia with an intact ventricular septum, and 6.4% for pulmonary atresia with ventricular septal defect. No children with secundum atrial septal defect, patent ductus arteriosus, or pulmonic stenosis have had infective endocarditis after surgery.

Conclusion.—The continuing incidence of endocarditis after surgery for congenital heart defect, particularly valvular aortic stenosis, merits education about endocarditis prophylaxis for children and adults with repaired congenital heart defects.

THE INCIDENCE OF infective endocarditis is rare and is estimated to be 0.38 case per 10,000 person-years. Over the last 2 decades, a changing pattern of occurrence of infective endocarditis has been noted, in part owing to a decrease in the case-fatality rate, a shift to more uncommon causative organisms, an improvement in diagnostic methods, and the growing proportion of cases in individuals who have had surgery for congenital heart disease. Although case series of children with endocarditis have been reported, these studies could not estimate the incidence of endocarditis after surgery for a congenital heart defect. It is well understood that the presence of a heart defect increases this incidence, particularly defects associated with high-velocity or turbulent flows, such as ventricular septal defect (VSD), aortic stenosis, coarctation of the aorta, and patent ductus arteriosus (PDA). Conversely, defects such as secundum atrial septal defects (ASDs) are not associated with infective endocarditis.

The risk of infective endocarditis should be eliminated or markedly decreased for heart defects that can be completely repaired surgically such as ASDs, VSDs, and PDA. For other defects, such as aortic valve disease, that risk may not be markedly altered by surgery. For some complex defects, the risk of infective endocarditis may actually be increased by surgery by placement of a prosthetic valve or conduit or with palliative shunt surgery for complex cyanotic heart disease.

Over the last 15 years, we have prospectively followed up all Oregon residents with any of 12 congenital heart defects for morbidity and mortality as part of a registry. The purpose of this analysis was to demonstrate the incidence of endocarditis in patients with congenital heart disease after surgical repair in a population-based cohort. The estimation of comparative risks among different defects will allow prevention to focus on individuals who are at highest risk after surgery.

METHODS

In 1982, we instituted a population-based registry to enroll all Oregon residents who had surgical repair of major congenital heart defects at less than 19
years of age from 1958 to the present. Surgery was performed at 5 Oregon hospitals: 0.7% of these procedures occurred at hospitals outside Oregon. Over time, this registry has been expanded to include 12 major heart defects: (1) tetralogy of Fallot; (2) isolated VSD; (3) isolated secundum ASD; (4) coarctation of the aorta with or without VSD or aortic valve disease; (5) aortic stenosis including isolated valvular, subaortic, and supravalvular aortic stenosis; (6) isolated pulmonary valvular stenosis with intact ventricular septum; (7) dextrotransposition of the great arteries; (8) isolated PDA in children older than 3 months to exclude PDA associated with prematurity; (9) primum ASD with left atrioventricular septal defect (AVSD); (10) complete atrioventricular septal defect (AVSD); (11) pulmonary atresia with intact ventricular septum; and (12) pulmonary atresia with VSD (tetralogy of Fallot with pulmonary atresia). Children with PDA or patent foramen ovale associated with these defects are included in the cohort.

Children who had palliative surgery only are excluded from this cohort. However, children who had placement of a systemic-to-pulmonary shunt or pulmonary artery banding are included if subsequent definitive surgery was performed. For inclusion in this registry, definitive surgical repair of tetralogy of Fallot is defined as closure of the VSD and relief of pulmonary valvular and right ventricular outflow tract obstruction. For VSD and primum and secundum ASD, the defect was closed by a prosthetic patch or suture; repair of the mitral cleft is usually included in repair of primum ASD. Repair for relief of coarctation of the aorta has varied by aortic anatomy, surgical preference, and year of surgery; a small number with balloon dilatation of native coarctation has been included. Surgical procedures for coarctation have included end-to-end anastomosis, bypass graft (ie, ascending-descending conduit), subclavian flap aortoplasty, and prosthetic patch aortoplasty. Initial procedures for relief of aortic stenosis included valvotomy in 96%, aortic valve replacement in 2%, and balloon valvotomy in 2%. For pulmonary stenosis, 82% had surgical valvotomy, and 18% had balloon valvotomy. Repair of transposition of the great arteries has changed from the Mustard repair, which was used until 1982, to the Senning technique, and more recently to arterial switch. Patent ductus arteriosus was repaired by ligation, division, or both. Complete AVSD repair includes closure of the atrial and ventricular septa and repair of the mitral valve. Repair of pulmonary atresia includes establishment of right ventricular to pulmonary artery continuity; when associated with VSD, this also includes closure of the defect.

To form the registry, medical records departments in all Oregon hospitals that performed cardiac or thoracic surgery were asked to identify cases using both procedure and diagnostic codes of hospital admissions. Computerized records, card files of hospital admissions, and surgical logs were searched to identify cases. Since 1982, data have been added to the registry prospectively with yearly ascertainment of surgical cases. Chart abstraction was performed by the principal investigator or a research assistant who had undergone training and monitoring to maintain data quality and integrity. To obtain long-term follow-up information, subjects were traced through next of kin, physicians, employment records, Department of Motor Vehicles registrations, city and telephone directories, and the National Death Index. Follow-up status of all individuals in the registry was determined by a mailed questionnaire every 2 years; data from the follow-up cycle that began in late 1993 are included in this analysis. Individuals who did not complete the mailed questionnaire were contacted by telephone for a formatted interview. In addition to assessing functional status, the questionnaire asked the individual or their family about specific events such as endocarditis, recurrent surgery, or any hospitalization. Affirmative answers to endocarditis and all hospitalizations for cardiac or infection-related events were confirmed through medical records or patient’s physicians. Death certificates or hospital records of all deaths were obtained. Prior to surgery, endocarditis was identified at the time of inclusion into the registry. Endocarditis was considered to be present if the medical records indicated (1) histologic evidence of endocarditis from surgery or autopsy; (2) positive blood culture and new or changing regurgitant murmur, development of congestive heart failure, vegetation on echocardiogram, or vascular phenomena; or (3) negative blood culture with fever and new or changing regurgitant murmur, vegetation on echocardiogram, or vascular phenomena. Only 1 case of physician-diagnosed endocarditis did not meet any of these 3 criteria.

The cumulative incidence of postoperative endocarditis for each defect cohort was estimated by the Kaplan-Meier method. This was defined as elapsed time from the date of surgery to the date of endocarditis or, in subjects free of endocarditis, the date of death or the last date of contact with the subject. Annualized risk was calculated by dividing the total number of cases of endocarditis into the total years of follow-up after surgery for each cohort. All statistics were calculated separately for each defect cohort and are presented as the proportion (and SE) with endocarditis.

RESULTS

The cohorts included in this analysis comprise 3860 individuals who had surgery for 1 of 12 heart defects. Secundum ASD was the most common defect, and pulmonary atresia the least common. The sample size, median age at operation, and total patient-years of follow-up after surgery are shown in Table 1. In this population, 90.8% were non-Hispanic white, 4.0% Hispanic, 2.3% Asian or Pacific Islander, 2.1% African American, and 0.8% Native American. The median age at operation ranged from 0.005 year (2 days) for pulmonary atresia to 7.0 years for aortic valve stenosis; however, the age of surgery has decreased over time, as previously described for this cohort. Most recently, the median age at reparative surgery for tetralogy of Fallot has been 7.2 months, 10.8 months for VSD, 3.0 months for coarctation of the aorta, 4.9 years for aortic stenosis, 8.4 months for pulmonary valve stenosis, and 11 days for transposition of the great arteries.

Follow-up data for endocarditis were available from 88% of this population through 1993. The highest rate of follow-up was in the cohort with transposition
of the great arteries (95%), and the lowest rate was for those with PDA (84%). The median follow-up duration was longest for the cohort with tetralogy of Fallot at 159 months and shortest for the cohort with pulmonary atresia at 8 months, owing in part to a high rate of operative mortality in this latter group.

Prior to definitive surgery, infective endocarditis occurred most often in children with VSD and tetralogy of Fallot with a systemic-to-pulmonary shunt. In the 98 children with tetralogy of Fallot who had a palliative shunt, 4 cases occurred for a risk of 8.2 cases per 1000 patient-years (Table 2); no cases occurred in the first year after shunt placement. Prior to surgical closure of the VSD, the incidence (SE) of infective endocarditis was 1.1% (0.7%) at 5 years of age; overall, the risk was 3.8 cases per 1000 patient-years prior to surgical closure (Table 2). Single cases of endocarditis were noted in the cohort with valvular aortic stenosis, pulmonary atresia with VSD, and PDA prior to definitive surgery. No children with primum or secundum ASD, coarctation of the aorta, pulmonary valve stenosis, transposition of the great arteries, complete AVSD, or pulmonary atresia had infective endocarditis prior to operative repair.

In the 30 years after repair of secundum ASD, pulmonary valve stenosis, and PDA, no one has developed infective endocarditis (Tables 2 and 3). After surgery, the highest incidence of infective endocarditis has been in the cohort with aortic valve stenosis (Table 3). This rate excludes individuals with isolated supravalvular (n=18) or subvalvular aortic stenosis (n=36) in whom there were no cases of infective endocarditis either before or after surgery. Thirteen cases of infective endocarditis were diagnosed after surgery for aortic valve stenosis. The incidence of infective endocarditis appears to increase more rapidly after 5 years of follow-up after surgery, and by 25 years the cumulative incidence is 13.3% (3.8%) (Table 3). Considered over all years of follow-up, the risk of infective endocarditis is 7.2 cases per 1000 patient-years (Table 2).

To determine if valve replacement increased the risk of endocarditis in the cohort with aortic stenosis, we compared this with the risk with a native valve (Figure). The incidence with a native valve was computed using the time of valvotomy to time of valve replacement or the last date of observation. Incidence with a prosthetic valve was computed from time of valve replacement to the last observation. In total, 16% of the cohort had aortic valve replacement either as their initial surgery (n=2) or at reoperation (n=26). With a prosthetic valve, there were 3 cases of endocarditis with a 10-year incidence of 26% (13%). With a native valve, there were 10 cases with a 10-year incidence of 5% (2%), 20-year incidence of 11% (4%), and 25-year incidence of 15% (6%).

In the cohort with coarctation, infective endocarditis occurred in 8 individuals after surgery. In all cases, the infection occurred either at the site of repair or at an associated abnormal aortic valve, with or without stenosis; in 3, infective endocarditis occurred immediately after surgery for coarctation. As with valvular aortic stenosis, the risk appears to increase with age or time after surgery. By 30 years after surgery, the cumulative incidence of endocarditis is 3.5% (Table 3). Over all years of follow-up, the risk is 1.2 cases per 1000 patient-years (Table 2).

Five individuals with tetralogy of Fallot had infective endocarditis after reparative surgery. All cases occurred within the first decade after surgery; at 10 years after surgery the cumulative incidence of endocarditis is 1.3% (0.6%), which remains constant through 30 years (Table 3). Three of the 5 patients with infective endocarditis had a residual VSD; one of these individuals was presumed to have acquired infective endocarditis after a cardiac catheterization. One case occurred in the immediate postoperative period, and another had an infected prosthetic right outflow tract patch.

In the group with pulmonary atresia with VSD, there were 3 episodes of infective endocarditis after reparative surgery; 2 of the 3 had a pulmonary homograft. At 10 years after surgery, 6.4% of the cohort had an episode of infective endocarditis (Table 3); 2 episodes occurred immediately postoperatively. One episode occurred in a child with pulmonary atresia without VSD 1 month after surgery.

After surgery for VSD, infective endocarditis occurred in 4 individuals. At 30 years after surgery, the cumulative incidence is 4.1% (Table 3). This risk appears to increase 20 years after surgical closure of the defect. Two of these 4 individuals had a residual VSD; 2 others had no residual VSD but 1 had a bicuspid aortic valve and the other developed aortic insufficiency after VSD repair. No one with a closed VSD in the absence of other anomalies developed endocarditis. Two cases of infective endocarditis occurred after repair of primum ASD, 1 in the immediate postoperative period. At 20 years after surgery, the incidence was 2.8% (Table 3). Only 1 child developed infective endocarditis after complete AVSD repair; the 15-year incidence rate is 1.1% (Table 3). After repair of dextrotransposition of the great arteries, 1 individual developed endocarditis, which resulted in his death 16 years after a Mustard procedure. No cases of endocarditis occurred after Senning or arterial switch procedures in this cohort.

The causative organism was identified in 92% of cases. A positive blood culture was present in 33 of 38 cases of endocarditis that occurred after surgery; 3 were consistently culture negative, and in 2 the diagnosis was first considered at autopsy. Because endocarditis was diagnosed as early as 1962 in this cohort, the method of diagnosis has differed over time. In 26% of the cases, echocardiography was not used. Of those with an echocardiogram, findings indicative of

| Table 2.—Annualized Risk of Endocarditis Within This Population |
|---------------------------------|-----------------|-----------------|
| **Risk for Endocarditis**       | **No. of Cases per 1000 Patient-Years** |
| High Pulmonary atresia with ventricular septal defect | 11.5 |
| Tetralogy of Fallot with palliative systemic-to-pulmonary shunt | 8.2 |
| Aortic valve stenosis*          | 7.2 |
| Pulmonary atresia*              | 6.4 |
| Unoperated ventricular septal defect | 3.8 |
| Moderate to low                 |                |
| Primum atrial septal defect with cleft mitral valve* | 1.8 |
| Coarctation of the aorta*       | 1.2 |
| Complete atrioventricular septal defect* | 1.0 |
| Tetralogy of Fallot*            | 0.7 |
| Dextrotransposition of the great arteries* | 0.7 |
| Ventricular septal defect†      | 0.6 |
| No documented risk              |                |
| Atrial septal defect*           | 0 |
| Patent ductus arteriosus*       | 0 |
| Pulmonic stenosis*              | 0 |

*After definitive surgical repair. For pulmonary atresia, this represents establishment of right ventricle to pulmonary artery continuity.
†All cases of endocarditis occurred either with a residual ventricular septal defect or with associated aortic valve anomalies including bicuspid aortic valve and aortic insufficiency. No cases of endocarditis occurred with closed ventricular septal defect in the absence of other anomalies.
endocarditis were present in 54%. The most common infecting organisms were *Streptococcus viridans* and *Staphylococcus aureus*(each 23% of total); coagulase-negative staphylococci, β-hemolytic streptococci, or *Staphylococcus epidermidis* infection (each 9%); and single cases of *Candida*, *Serratia*, and both *S aureus* and *S viridans* infection.

Overall, of the 38 cases of endocarditis after surgical repair, there were 7 deaths from endocarditis (18%). These deaths were distributed among different heart defects. Endocarditis occurred in the immediate postoperative period in 22% and from infected patch material in 6%. The infection was presumed by the treating physician to be of dental origin in 14% based on a recent dental procedure or poor oral hygiene. Single episodes of endocarditis were presumed to be from a ventriculoperitoneal shunt, a Pott shunt, cardiac catheterization, skin laceration, acne, and intravenous drug abuse. The route of infection was unclear in 32%.

**COMMENT**

In contrast to previous studies that have analyzed the frequency of heart defects in a case series of individuals with endocarditis, our analysis prospectively determined the occurrence of endocarditis in groups with specific heart defects after surgery. This approach allows computation of the long-term risk of endocarditis for specific heart defects and a direct comparison of this risk among subpopulations. As the population of adults with congenital heart defects increases in number owing to the dramatic improvement in operative survival over the last 40 years, it is likely that endocarditis will play a significant role in morbidity and mortality in this population.

Table 2 summarizes the risk of developing endocarditis categorized by the clustering of risk apparent in this cohort. Table 3 shows the risk of endocarditis for specific heart defects. This reflects risk over all years after surgical repair. It should be noted that endocarditis within the immediate postoperative period explained 22% of the cases, occurring in children with tetralogy of Fallot, primum ASD, coarctation, pulmonary atresia, and pulmonary atresia with intact septum. Endocarditis in this period does not markedly alter the risk over time or the comparative risk among these groups, except for pulmonary atresia, as endocarditis continued to occur after this period. This emphasizes the importance of antibiotic prophylaxis. Because of the frequent use of prosthetic conduits with pulmonary atresia, these individuals likely continue at high risk of endocarditis after the immediate operative period.

The highest incidence of endocarditis after long-term follow-up is for those with left-sided outflow obstruction; for example, for aortic valvular stenosis the incidence rises to 20.6% after 30 years (Table 3). The risk of endocarditis in this group has been cited as 1.6 cases per 1000 patient-years in those treated medically, but 4.1 cases per 1000 patient-years with surgical treatment. In the present study, the annualized risk with aortic stenosis is somewhat higher at 7.2 cases per 1000 patient-years (Table 2). This study appears to confirm a higher rate of infective endocarditis with a prosthetic valve as compared with a native valve with aortic stenosis. However, this finding must be interpreted with caution.
caution as individuals contributed time to both cohorts. For coarctation of the aorta, the risk is more moderate at 1.2 cases per 1000 patient-years (Table 2). In the majority of these individuals, the site of infection was an anatomically abnormal aortic valve, a well-recognized association.

In contrast, the occurrence of endocarditis is low with right-sided heart defects, particularly tetralogy of Fallot. In all individuals who developed infective endocarditis after repair of tetralogy, either a residual VSD was present or the prosthetic patch or a Pott shunt was the source of infection. Surgery is known to reduce the risk of infective endocarditis for children with tetralogy of Fallot; these data indicate that with complete closure of the VSD and without systemic-to-pulmonary shunt, this risk may be very small. The higher occurrence of endocarditis with pulmonary atresia with VSD at 11.5 cases per 1000 patient-years (Table 2) likely results from the placement of a prosthetic conduit. This estimate must be interpreted with caution given the small cohort size and relative paucity of years of follow-up.

The incidence of infective endocarditis in this population-based cohort is likely to be representative of the larger population after definitive surgery for these defects. However, this may underestimate the true incidence given the reliance on self-reporting from mailed questionnaires or interviews. We have taken great efforts to minimize this by following a high percentage of the cohort, and by obtaining information from multiple sources through inquiries about endocarditis, hospitalizations, and valve replacement; some cases may have been missed because no autopsy was performed. Conversely, it is also possible that the incidence is overestimated, given a higher diagnostic suspicion in a patient with a heart defect who presents with bacteremia. Nonetheless, we do not believe that the risks of infective endocarditis in this study substantially misrepresent the true occurrence, particularly in the cohorts with the largest sample sizes.

With changes in diagnostic methods over the time of this study, it is impossible to determine the endocarditis risk of specific anatomic or physiologic variants, such as with mitral regurgitation after primum ASD repair or bicuspid aortic valve with coarctation. It is possible that endocarditis risks for a cohort may be dependent on such variants. These data are also generalized from surgical procedures performed over more than 35 years; it is possible that changes in surgical strategy may alter these risks somewhat. Despite this, the strength of these data is in the population database, prospective determination, and long period of follow-up.

Unfortunately, this study cannot address the issue of antibiotic prophylaxis in a population with repaired congenital heart defects. Given the limitations of observational data, it is impossible to determine if the use or lack of use of antibiotic prophylaxis had any effect on incidence. The American Heart Association recommendations support use of endocarditis prophylaxis for individuals in all heart defect cohorts included in this study except for isolated secundum ASD and for VSD and PDA more than 6 months after surgical repair without residua. The European consensus statement is in agreement except that it does not include pulmonary stenosis on the list of defects for which endocarditis prophylaxis is recommended. These data support the risks and concomitant recommendations for prophylaxis suggested in both statements with regard to no risk associated with secundum ASD and with VSD and PDA after surgical repair and the European consensus as to no risk with pulmonic stenosis. Longer follow-up from this and larger data sets will need to confirm no risk associated with pulmonic stenosis.

Perhaps the most important outcome of this study is the recognition of a high risk of endocarditis with aortic stenosis. As such, greater efforts should be made to educate individuals with defects that place them at high risk for endocarditis, as well as others participating in their health care. In a previous study of parental knowledge of endocarditis prophylaxis, 98% of parents knew the name of their child’s heart condition but only 56% of parents with at-risk children knew measures to prevent endocarditis. In a survey of adults with congenital heart disease seen in a special cardiology clinic, 68% correctly identified their heart condition and 79% knew that they needed to take an antibiotic prior to dental work. Education should begin with the parents of children as to the risk of infective endocarditis and the appropriate use of antibiotic prophylaxis. As individuals become adolescents, they should receive adequate information so that as adults, they will have a greater understanding of their heart disease and the importance of prevention of endocarditis.

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References