Outcome and performance of bioprosthetic pulmonary valve replacement in patients with congenital heart disease

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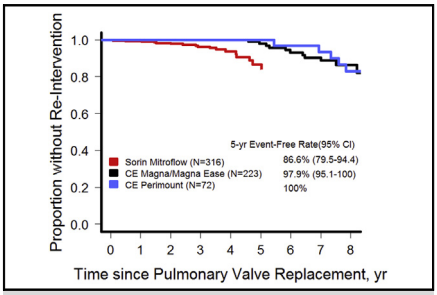
ABSTRACT

Objectives: The goal of this single-center series was to assess differences in reintervention by the type of valve used for surgical bioprosthetic pulmonary valve replacement and to identify independent predictors of reintervention.

Methods: Data were retrospectively collected for 611 patients undergoing pulmonary valve replacement from 1996 to 2014. Kaplan–Meier estimation and Cox proportional hazards regression methodologies were used.

Results: The median age of patients was 17.8 years (interquartile range, 11.9-27.3). The diagnosis was tetralogy of Fallot in 69% of patients. The median follow-up was 3.0 years (interquartile range, 1.1-5.3). Valve types included Sorin Mitroflow (Milan, Italy), 316 (50%; median age 16.5 years); Carpentier-Edwards (Irvine, Calif) Magna/MagnaEase, 223 (35%; median age, 19.3 years); and Carpentier-Edwards Perimount, 72 (11%; median age, 21.9 years). Reintervention occurred in 6.7% of patients (41/633) and was higher in children than adults (hazard ratio, 4.8). Age-adjusted 5-year reintervention rates were Sorin Mitroflow, 13.4%; Carpentier-Edwards Magna/MagnaEase, 2.1%; and Carpentier-Edwards Perimount, 0%. Reintervention was not associated with gender, valve insertion method, or concurrent procedures. The only independent risk factor for reintervention after controlling for age was valve type ($P < .001$). The Sorin Mitroflow valve had a shorter time to reintervention than the other 2 valve types (hazard ratios both >7, each $P < .001$). Differences by valve type did not depend on age (interaction $P = .61$).

Conclusions: Bioprosthetic pulmonary valve replacement in patients with congenital heart disease has excellent short-term outcomes, but children have an approximately 5-fold greater risk of reintervention than adults. Independently of age, reintervention rates vary by valve type. These differences may be important in valve selection and follow-up. (J Thorac Cardiovasc Surg 2016;152:1333-42)



Age-adjusted freedom from reintervention by valve type.

Central Message

Reintervention rates after bioprosthetic PVR vary by age and valve type, affecting valve choice and follow-up.

Perspective

Longer-term outcomes and optimal valve type for PVR in the pediatric population are unknown. All measures related to younger patient age at surgery were risk factors for reintervention. The association of age at surgery with time to reintervention was independent of valve type. The Sorin Mitroflow valve (Milan, Italy) was a significant age-adjusted risk factor for reintervention relative to the other valve types.

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Survival of children with congenital heart disease (CHD) has improved significantly over the last 15 years with advances in surgical techniques and perioperative care, leading to more adults with CHD than children. As a result, there is an increasing number of adolescents and adults undergoing pulmonary valve replacement (PVR) procedures. Current indications for PVR include asymptomatic and symptomatic patients with increased risk for right ventricular dilation and dysfunction, exercise intolerance, arrhythmia, and sudden cardiac events. Patients with tetralogy of Fallot (TOF) frequently develop severe pulmonary regurgitation after initial right ventricular outflow tract (RVOT) repair, and placement of bioprosthetic valves has demonstrated significant improvements in right ventricle

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Abbreviations and Acronyms

BMI = body mass index
BSA = body surface area
CE = Carpentier-Edwards
CHD = congenital heart disease
CI = confidence interval
HR = hazard ratio
MRI = magnetic resonance imaging
PVR = pulmonary valve replacement
RV = right ventricle
RVOT = right ventricular outflow tract
TOF = tetralogy of Fallot

(RV) function and exercise tolerance in these patients.[1,2] Bovine pericardial bioprosthetic valves in the aortic position in adults have demonstrated excellent short- and mid-term results, but many fail long term because of calcification resulting in increased leaflet rigidity.[3] However, longer-term outcomes and optimal valve type for PVR in the pediatric population are unknown. Our objective was to compare reintervention rates among different bioprosthetic valve types in patients with CHD undergoing PVR and to determine whether additional independent risk factors exist.

MATERIALS AND METHODS

This was an institutional review board–approved retrospective review of all patients with CHD who underwent bioprosthetic PVR at Boston Children's Hospital between January 1, 1996, and February 28, 2014. The data of 611 patients undergoing bioprosthetic PVR at Children's Hospital Boston were included. The primary end point was reintervention on the pulmonary valve and defined as a surgical procedure for valve replacement or a cardiac catheterization intervention for valve replacement (for insertion of a Melody [Medtronic Inc, Minneapolis, Minn] bovine jugular valve).

Demographics collected include date of birth, sex, intraoperative height, weight, and body surface area (BSA). Patient history includes the patient's primary diagnosis, and previous interventions including PVR(s), Ross procedure, internal cardiac defibrillator, pacemaker, catheterization, most recent type of RVOT, and relevant procedures. Surgical data were obtained from operative notes. Variables of interest include the date of admission, date of PVR procedure, indication for PVR, date of discharge, morbidity, and any complications before discharge. In addition, the specific valve type, valve size, valve insertion methods, and concomitant procedures were recorded.

The last date of follow-up record included in this study was July 30, 2014. Follow-up includes date of most recent follow-up, echocardiogram reports, and magnetic resonance image reports obtained as part of a routine examination. More specifically, data from echocardiogram reports will include the date of echocardiogram, estimated RV pressure gradient, maximum RVOT pressure gradient, and degree of pulmonary stenosis, pulmonary regurgitation, tricuspid regurgitation, RV dysfunction, and left ventricular dysfunction.

Definitions

BSA was calculated using the Haycock formula: $0.024265 \times \text{weight}^{0.5378} \times \text{height}^{0.3964}$. When height was not available, BSA was calculated from weight only: $0.1*(\text{weight}^{0.6667})$. Weight-for-age and body mass index (BMI)-for-age z scores and percentiles were calculated for the 371 patients aged less than 20 years using the Centers for Disease Control reference standard. A z score represents the number of standard deviation units the measurement is away from the mean of a healthy individual (mean z score of zero). Valve internal diameter dimensions were directly measured, and valve orifice area was calculated as the valve circumference: $3.14159 \times (0.5 \times \text{measured internal diameter})$.[2]

Statistical Methods

We compared patient characteristics by valve type using the chi-square test for categoric variables, analysis of variance for continuous variables with symmetric distributions, and Kruskal–Wallis test for other variables. Descriptive statistics used were frequency and percentage for categoric variables, mean ± standard deviation, and median with interquartile range for continuous variables. Dichotomous weight and BMI z scores were created to assess very small body size relative to age (z score <-2) and larger body size relative to age (z score >1).

Kaplan–Meier methodology and the log-rank test were used to estimate time to reintervention and compare unadjusted reintervention rates. Follow-up time was censored at the latest known follow-up or death. Cox proportional hazards regression was used to estimate covariate-adjusted associations between time to reintervention and valve type.

Candidate predictors for multivariable Cox proportional hazards regression with a stepwise selection procedure included labeled valve size, valve orifice area, weight, BSA, native RV outflow tract, and concurrent surgical procedure variables that had a univariate P value less than .20. Age at surgery and valve type were fixed in the multivariable model before applying the selection procedure. The criterion for entry of other variables into the multivariable model was $P < .15$, and the criterion to remain in the model was $P < .05$. The selected model was then refined as needed to account for differences in the complete-case dataset and the maximum sample size dataset.

Estimates of age-adjusted freedom from reintervention by valve type were obtained by the method of direct adjustment, fitting a stratified Cox proportional hazards model with a differing baseline hazard for each valve type and averaging the event-free probability estimates across all observations (of varying ages) at a given follow-up time. The estimates and confidence intervals (CIs) were calculated in SAS (SAS Institute, Inc, Cary, NC) using the method of Zhang and colleagues.[4] Analyses were performed using SAS version 9.4 and R version 3.2.1.

RESULTS

Patient Characteristics

Patient characteristics by valve type are shown in Table 1. Of the 611 patients who underwent bioprosthetic PVR between 1996 and 2014 (Figure E1), the valve type used was the Sorin Mitroflow (Milan, Italy) (LXA nontreated), 316 (50%); the Carpentier-Edwards (CE) (Irvine, Calif) Magna or MagnaEase, 223 (35%); and the CE Perimount, 72 (11%). The median age at surgery was 17.8 years (interquartile range, 11.9-27.3 years), and 50% of patients were aged less than 18 years ($P < .001$ across valve types). Only 8 patients were infants, and none were neonates. Patients receiving a Sorin Mitroflow were younger (median, 16.5 years) than those who received the CE Magna/MagnaEase (19.3 years) and CE Perimount valves (21.9 years).

The Sorin Mitroflow valves were implanted in patients in 2008 or later, in contrast to CE Perimount valves that were mostly all implanted in patients before 2006. Pulmonary