Reintervention rates after bioprosthetic pulmonary valve replacement in patients younger than 30 years of age: A multicenter analysis

Christopher W. Baird, MD,[a,b] Mariana Chávez, MD,[a] Lynn A. Sleeper, ScD,[b,c] Michele J. Borisuk, MSN, CPNP,[a] Emile A. Bacha, MD,[d] Luke Burchill, MD,[e] Kristine Guleserian, MD,[f] Michel Ilbawi, MD,[g] Khanh Nguyen, MD,[h] Anees Razzouk, MD,[i] Takeshi Shinkawa, MD,[j] Minmin Lu, MS,[c] and Stephanie M. Fuller, MD, MS[k]

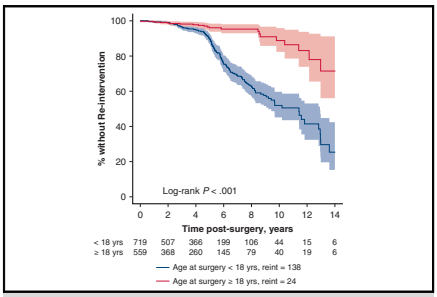
ABSTRACT

Objectives: To assess the difference in time to and predictors of reintervention according to valve type in surgical bioprosthetic pulmonary valve replacement (PVR) in patients younger than 30 years of age from multiple centers.

Methods: Data were retrospectively collected for 1278 patients <30 years of age undergoing PVR at 8 centers between 1996 and 2015.

Results: Mean age at PVR was 19.3 ± 12.8 years, with 719 (56.3%) patients ≤18 years of age. Diagnosis was tetralogy of Fallot in 626 patients (50.5%) and 165 (12.9%) had previous PVR. Median follow-up was 3.9 years (interquartile range, 1.2, 6.4). Multiple valve types were used, most commonly CE PERIMOUNT, 488 (38.2%), CE Magna/Magna Ease, 361 (28.2%), and Sorin Mitroflow 322 (25.2). Reintervention occurred in 12.7% and was most commonly due to pulmonary stenosis (68.8%), with most reinterventions occurring in children (85.2%) and with smaller valve sizes ($P < .001$) Among adults aged 18 to 30 years, younger age was not a significant risk factor for reintervention. Surgical indication of isolated pulmonary regurgitation was associated with a lower risk of reintervention ($P < .001$). Overall, 1-, 3-, 5-, and 10-year freedom from reintervention rates were 99%, 97%, 92%, and 65%. The only independent risk factors for reintervention after controlling for age and valve size were lack of a concomitant tricuspid valve procedure ($P = .02$) and valve type ($P < .001$); Sorin and St Jude valves were associated with similar time to reintervention, and deteriorated more rapidly than other valve types.

Conclusions: In this large multicenter study, 8% of patients have undergone reintervention by 5 years. Importantly, independent of age and valve size, reintervention rates vary by valve type. (J Thorac Cardiovasc Surg 2021;161:345-62)



Freedom from reintervention estimated probability by valve type, $P < .001$.

CENTRAL MESSAGE

Bioprosthetic PVR has acceptable outcomes. Younger age and smaller valve are independent predictors of a shorter time to reintervention. Different valve types have different rates of reintervention.

PERSPECTIVE

Due to early failure of homograft valves, bioprosthetic PVR has become more common in patients with CHD and has been shown to have excellent short-term outcomes. However, longer-term durability remains problematic. The goal of this multicenter study was to compare multiple valve types in patients younger than 30 years old undergoing PVR.

See Commentaries on pages 363, 364, and 365.

From the Departments of [a]Cardiac Surgery and [c]Cardiology, Boston Children's Hospital, Boston, Mass; [b]Department of Pediatrics, Harvard Medical School, Boston, Mass; [d]New York-Presbyterian/Columbia University Medical Center, New York, NY; [e]University of Melbourne Royal University Hospital, Melbourne, Australia; [f]Nicklaus Children's Hospital, Miami, Fla; [g]Rush University Medical Center, Chicago, Ill; [h]Maria Fareri Children's Hospital, Valhalla, NY; [i]Loma Linda University, Loma Linda, Calif; [j]Arkansas Children's Hospital, Little Rock, Ark; and [k]Children's Hospital of Philadelphia, Philadelphia, Pa.

This work was supported by an Edwards Lifesciences Grant.

Read at the 99th Annual Meeting of The American Association for Thoracic Surgery, Toronto, Ontario, Canada, May 4-7, 2019.

Received for publication May 8, 2019; revisions received June 9, 2020; accepted for publication June 10, 2020; available ahead of print Sept 10, 2020.

Address for reprints: Christopher W. Baird, MD, Harvard Medical School, 300 Longwood Ave, Boston, MA 02115 (E-mail: christopher.baird@childrens.harvard.edu).

0022-5223/$36.00

https://doi.org/10.1016/j.jtcvs.2020.06.157

Abbreviations and Acronyms

BSA = body surface area
CE = Carpentier-Edwards
CHD = congenital heart disease
CI = confidence interval
HR = hazard ratio
IQR = interquartile range
PR = pulmonary regurgitation
PS = pulmonary stenosis
PV = pulmonary valve
PVR = pulmonary valve replacement
RV = right ventricle

Scanning this QR code will take you to the article title page to access supplementary information. To view the AATS Annual Meeting Webcast, see the URL next to the webcast thumbnail.

Survival of children with congenital heart disease (CHD) has significantly improved with advances in surgical techniques and perioperative care, leading to more adults with CHD undergoing pulmonary valve replacement (PVR). Due to early homograft valve failure,[1] bioprosthetic PVR has become more common and has been shown to have excellent short-term outcomes.[2,3] However, longer-term durability remains problematic, with more than 80% valve dysfunction and failure reported at 10 years.[4] In addition, children have a significantly greater risk of early reintervention compared with adults.[5,6] Furthermore, independent of age, reintervention rates vary by valve type.[7] However, most reports in children have been based on single-center data and may not be generalizable. Multicenter long-term outcomes and optimal valve type for PVR in the pediatric population are unknown. Our objective was to assess differences in time to reintervention and identify independent factors by the type of valve used for surgical bioprosthetic PVR in the recent era.

METHODS

This was a multi-institutional review board–approved (IRB-P00023154, approval date: June 29, 2016) retrospective review of all patients with CHD who underwent bioprosthetic PVR between February 1996 and July 2015 from 8 centers, including Advocate Medical Center (Chicago, Ill); Arkansas Children's Hospital (Little Rock, Ark); Boston Children's Hospital (Boston, Mass), Children's Hospital of Philadelphia (Philadelphia, Pa); Dallas Children's Hospital (Dallas, Tex); Loma Linda (Los Angeles, Calif); Columbia (New York, NY); and Mt Sinai Medical Center (New York, NY).

Data were collected by a research team at each respective center and entered into a REDCap secure URL database (Vanderbilt University, Nashville, Tenn). The data were exported with all identifiers removed by a central study team at Boston Children's Hospital, which served as the managing site. The primary end point was reintervention on the pulmonary valve (PV) and defined as surgical or cardiac catheterization (for insertion of a Melody [Medtronic Inc, Minneapolis, Minn] bovine jugular valve) valve replacement. We did not analyze additional PVR on the same patients (Figure 1).

Demographics collected include date of birth, sex, intraoperative height, weight, and body surface area (BSA). Patient history included fundamental diagnosis and previous interventions including PVR. Surgical data were obtained from operative notes including valve type, size, insertion methods, and concomitant procedures. Variables of interest included the date of admission, date of PVR procedure, indication for PVR, date of discharge, morbidity, and complications before discharge.

Follow-up was recorded until October 2016 and included the following routine clinical care: date of most recent follow-up and echocardiogram reports (time from PVR, estimated right ventricular [RV] pressure gradient, maximum right ventricular outflow tract pressure gradient, and degree of pulmonary stenosis [PS], pulmonary regurgitation [PR], tricuspid regurgitation, RV dysfunction, and left ventricular dysfunction).

Definitions

BSA was calculated using the Haycock formula: $0.024265 * \text{weight}^{0.5378} * \text{height}^{0.3964}$. When height was not available, BSA was calculated from weight only: $0.1 * (\text{weight}^{0.6667})$. Valve internal diameter dimensions were directly measured, and valve orifice area was calculated as the valve circumference.

Statistical Methods

Descriptive statistics include mean ± standard deviation and median with interquartile range (IQR) for continuous variables. Categorical data were described as a frequency.

Patient characteristics by valve type were compared by using the Fisher exact test or χ^2 test for categorical variables, and analysis of variance or Kruskal–Wallis test for continuous variables.

Kaplan–Meier methodology and the log-rank test were used to estimate time to the outcome and compare unadjusted outcome rates. If reintervention did not occur, follow-up time was censored at the latest known follow-up or death. Cox regression modeling accounting for variation between study centers was used to estimate the association between time to the reintervention and candidate predictors, and in particular, to estimate covariate-adjusted associations between outcome and valve type. Piecewise linear functions were also fit for some covariates, such as age at surgery; the break points for the functions were identified with the use of generalized additive modeling. Stepwise selection was performed by including all variables with a univariate P value less than .20 in Table 4 as candidate predictors, with the exception of predischarge echocardiogram measures, to construct a multivariable Cox regression model accounting for center variation of factors that were independently associated with time to outcome. The criterion for entry into the multivariable model was $P < .15$ and the criterion to remain in the model was $P < .05$. The Uno concordance (c-) statistic for the model is reported. As a sensitivity analysis, we also constructed the multivariable model on the reduced cohort resulting from inclusion of the predischarge echo parameters (approximately 80% complete data) as candidates during model selection; model terms selected did not change.

Analyses were performed using SAS, version 9.4 (SAS Institute, Inc, Cary, NC) and R version 3.2.1 (R Foundation for Statistical Computing, Vienna, Austria).

RESULTS

Characteristics

A total of 1278 patients were included. Center characteristics including valve types implanted are shown in Table 1.

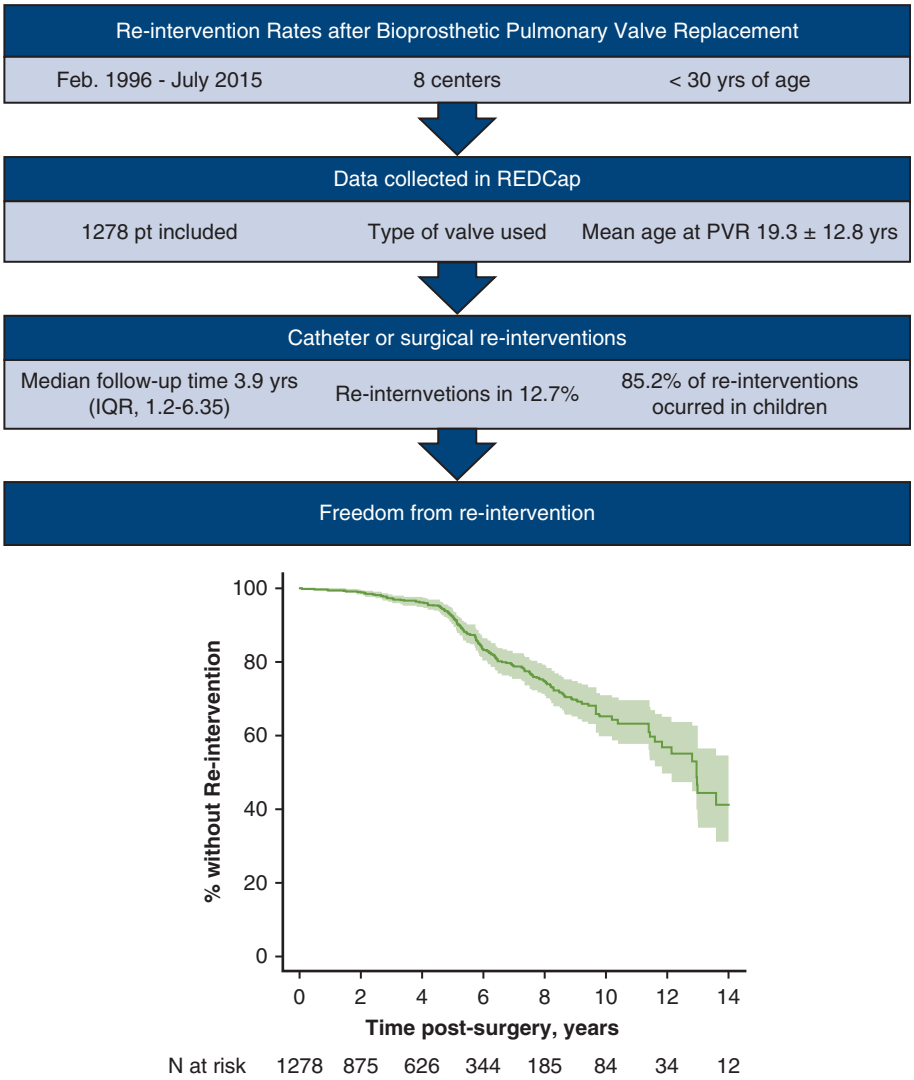


FIGURE 1. Data were retrospectively collected in all patients younger than 30 years of age who had surgery from February 1996 to July 2015 from 8 centers. Data were entered into a REDCap database and surgical or catheter-based reinterventions were captured. Kaplan–Meier curve shows overall estimated freedom from reintervention. The 5-year freedom from reintervention rate is 92% (95% CI, 90%-94%). *PVR*, Pulmonary valve replacement; *IQR*, interquartile range.

The following numbers of valves were implanted at each center: Advocate Medical Center, 192 (14%); Arkansas Children's Hospital, 237 (17%); Boston Children's Hospital, 661 (47%), Children's Hospital of Philadelphia, 103 (7%); Dallas Children's Hospital, 7 (0.5%); Loma Linda, 38 (2.7%); Columbia, 63 (5%); and Mt Sinai, 40 (2.9%). One-third (n = 427) of valve implants were performed before 2008.

Patient characteristics by valve type are shown in Table 1; 49% were male with fundamental diagnosis tetralogy of Fallot in 68%. PVR was the primary indication for surgery in 91% of cases. Median age at surgery was 16.7 (IQR, 10.6-24.5) years. More than one-half (56%, n = 719) of the patients were pediatric (<18.0 years). The valve types used were the Carpentier-Edwards (CE; Irvine, Calif); PERIMOUNT, 488 (38%); CE Magna/Magna Ease, 361 (28%) (Magna, 251 and Magna Ease, 110); Sorin Mitroflow (Milan, Italy; LXA nontreated), 322 (25%); St Jude, 54 (4%) (St Jude Epic, 49 and St Jude Biocor, 5); Hancock, 32 (2.5%); and other valve types, 21 (including Medtronic Mosaic, 5; CE porcine, 6; Medtronic melody, 7; and freestyle valves, 3). Among the 3 most commonly used valves, the majority (98%) of Mitroflow valves were implanted at a single center (Boston). CE PERIMOUNT and Magna/Magna Ease valves were distributed among all centers.

The median implanted valve size for most valves was 25 mm, with exceptions of the Hancock (20 mm) and the CE Magna/Magna Ease (27 mm). The median age at surgery was 16.7 years (IQR, 10.6-24.5 years), with 56% of patients aged <18 years ($P < .001$). There were no neonates.

TABLE 1. Patient characteristics overall and by valve type

Variables	Overall	Sorin Mitroflow	St Jude	CE PERIMOUNT	CE Magna/ Magna Ease	Hancock	Other	*P*
N	1278	322	54	488	361	32	21	
Valve type								
Medtronic Mosaic	5 (0.4%)						5	
Sorin Mitroflow	322 (25.2%)	322						
St Jude Epic	49 (3.8%)		49					
St Jude Biocor	5 (0.4%)		5					
CE PERIMOUNT	488 (38.2%)			488				
CE Magna	251 (19.6%)				251			
CE Magna Ease	110 (8.6%)				110			
Hancock	32 (2.5%)					32		
Melody	7 (0.5%)						7	
Freestyle	3 (0.2%)						3	
CE porcine	6 (0.5%)						6	
Year of surgery								**<.001**
Before 2008	427 (33.4%)	0 (0%)	3 (5.6%)	248 (50.8%)	136 (37.7%)	31 (96.9%)	9 (42.9%)	
2008 and later	851 (66.6%)	322 (100%)	51 (94.4%)	240 (49.2%)	225 (62.3%)	1 (3.1%)	12 (57.1%)	
Male sex	630 (49.3%)	134 (41.6%)	34 (63.0%)	276 (56.7%)	162 (44.9%)	16 (50.0%)	8 (38.1%)	**<.001**
Age at surgery, y								
Mean ± SD	19.3 ± 12.8	18.6 ± 12.7	18.5 ± 14.5	19.4 ± 12.5	21.1 ± 12.9	10.1 ± 9.2	13.2 ± 12.7	**<.001**
Median (IQR)	16.7 (10.6, 24.5)	16.4 (9.8, 22.6)	14.3 (10.0, 19.6)	16.8 (10.8, 24.9)	17.5 (12.6, 27.6)	7.8 (3.1, 15.0)	10.7 (2.7, 17.1)	**<.001**
Pediatric (<18 y)	719 (56.3%)	184 (57.1%)	36 (66.7%)	270 (55.3%)	184 (51.0%)	29 (90.6%)	16 (76.2%)	**<.001**
BSA, m^2	1.5 ± 0.5	1.5 ± 0.5	1.4 ± 0.5	1.5 ± 0.5	1.6 ± 0.5	1.0 ± 0.6	1.2 ± 0.8	
Fundamental diagnosis								**<.001**
1: TOF	626 (50.5%)	152 (47.4%)	28 (51.9%)	249 (53.9%)	180 (51.6%)	6 (18.8%)	11 (52.4%)	
2: TOF/PA	135 (10.9%)	58 (18.1%)	5 (9.3%)	26 (5.6%)	39 (11.2%)	6 (18.8%)	1 (4.8%)	
3: TOF/CAVC	21 (1.7%)	3 (0.9%)	1 (1.9%)	11 (2.4%)	4 (1.1%)	2 (6.3%)	0 (0%)	
4: TOF/absent PV	57 (4.6%)	13 (4.0%)	3 (5.6%)	23 (5.0%)	17 (4.9%)	1 (3.1%)	0 (0%)	
5: Pulmonary stenosis	156 (12.6%)	38 (11.8%)	9 (16.7%)	52 (11.3%)	53 (15.2%)	2 (6.3%)	2 (9.5%)	
6: Pulmonary atresia	75 (6.1%)	23 (7.2%)	3 (5.6%)	24 (5.2%)	19 (5.4%)	2 (6.3%)	4 (19.0%)	
7: Aortic stenosis	29 (2.3%)	4 (1.2%)	0 (0%)	16 (3.5%)	7 (2.0%)	0 (0%)	2 (9.5%)	
8: Truncus arteriosus	56 (4.5%)	16 (5.0%)	2 (3.7%)	24 (5.2%)	9 (2.6%)	5 (15.6%)	0 (0%)	
9: dTGA	22 (1.8%)	6 (1.9%)	1 (1.9%)	8 (1.7%)	5 (1.4%)	2 (6.3%)	0 (0%)	
10: Other	62 (5.0%)	8 (2.5%)	2 (3.7%)	29 (6.3%)	16 (4.6%)	6 (18.8%)	1 (4.8%)	
Unknown	39	1	0	26	12	0	0	
Previous PVR	165 (12.9%)	17 (5.3%)	9 (16.7%)	80 (16.4%)	44 (12.2%)	13 (40.6%)	2 (9.5%)	**<.001**
Type of outflow tract of primary operation								**<.001**
1: Native	122 (11.0%)	24 (7.5%)	5 (12.5%)	43 (11.8%)	46 (13.8%)	1 (3.2%)	3 (15.8%)	
2: RVOT/TP	736 (66.6%)	220 (69.0%)	31 (77.5%)	230 (63.4%)	240 (72.1%)	4 (12.9%)	11 (57.9%)	
3: Homograft	137 (12.4%)	61 (19.1%)	4 (10.0%)	37 (10.2%)	30 (9.0%)	1 (3.2%)	4 (21.1%)	
4: Valved tube	84 (7.6%)	8 (2.5%)	0 (0%)	40 (11.0%)	10 (3.0%)	25 (80.6%)	1 (5.3%)	
5: Nonvalved tube	23 (2.1%)	6 (1.9%)	0 (0%)	10 (2.8%)	7 (2.1%)	0 (0%)	0 (0%)	
6: Other	3 (0.3%)	0 (0%)	0 (0%)	3 (0.8%)	0 (0%)	0 (0%)	0 (0%)	
Unknown	122 (11.0%)	24 (7.5%)	5 (12.5%)	43 (11.8%)	46 (13.8%)	1 (3.2%)	3 (15.8%)	
At surgery								
Surgical indication(s)								
Pulmonary regurgitation	822 (64.3%)	205 (63.7%)	30 (55.6%)	304 (62.3%)	260 (72.0%)	12 (37.5%)	11 (52.4%)	**<.001**
Pulmonary stenosis	144 (11.3%)	24 (7.5%)	5 (9.3%)	56 (11.5%)	36 (10.0%)	17 (53.1%)	6 (28.6%)	**<.001**
PR/PS	239 (18.7%)	80 (24.8%)	14 (25.9%)	99 (20.3%)	42 (11.6%)	1 (3.1%)	3 (14.3%)	**<.001**

(Continued)

TABLE 1. Continued

Variables	Overall	Sorin Mitroflow	St Jude	CE PERIMOUNT	CE Magna/ Magna Ease	Hancock	Other	*P*
Endocarditis	9 (0.7%)	4 (1.2%)	2 (3.7%)	2 (0.4%)	1 (0.3%)	0 (0%)	0 (0%)	.07
Other	158 (12.4%)	20 (6.2%)	9 (16.7%)	64 (13.1%)	50 (13.9%)	12 (37.5%)	3 (14.3%)	**<.001**
PVR as primary indication for surgery	1157 (90.6%)	283 (87.9%)	46 (85.2%)	450 (92.4%)	331 (91.7%)	32 (100%)	15 (71.4%)	**.002**
Valve size, mm	25.0 ± 2.9	24.3 ± 2.5	24.1 ± 3.1	25.3 ± 2.7	25.7 ± 2.4	20.3 ± 4.3	22.4 ± 5.8	**<.001**
Valve size/BSA, mm/m^2								
N	1209	321	54	439	342	32	21	
Median (IQR)	16.4 (14.2, 22.1)	16.2 (14.0, 22.3)	17.3 (14.5, 21.3)	16.7 (14.5, 22.3)	16.1 (13.9, 19.7)	23.2 (15.4, 29.5)	26.6 (14.0, 31.0)	**.004**
Valve insertion method								**<.001**
Isolated with PA closure	183 (14.3%)	31 (9.6%)	3 (5.6%)	73 (15.0%)	70 (19.4%)	3 (9.4%)	3 (14.3%)	
Anterior patch	908 (71.2%)	237 (73.6%)	42 (77.8%)	343 (70.6%)	259 (71.7%)	12 (37.5%)	15 (71.4%)	
Dacron/ HEMASHIELD tube	129 (10.1%)	40 (12.4%)	2 (3.7%)	46 (9.5%)	25 (6.9%)	16 (50.0%)	0 (0%)	
Gore-Tex tube	43 (3.4%)	14 (4.3%)	2 (3.7%)	19 (3.9%)	7 (1.9%)	1 (3.1%)	0 (0%)	
Sinus of Valsalva graft	0	–	–	–	–	–	–	
Other	13 (1.0%)	0 (0%)	5 (9.3%)	5 (1.0%)	0 (0%)	0 (0%)	3 (14.3%)	
Unknown	2	0	0	2	0	0	0	
Combined procedures	925 (72.4%)	245 (76.1%)	45 (83.3%)	339 (69.5%)	259 (71.7%)	19 (59.4%)	18 (85.7%)	**.03**
LPA plasty	125 (9.8%)	33 (10.2%)	4 (7.4%)	46 (9.4%)	37 (10.2%)	4 (12.5%)	1 (4.8%)	.92
RPA plasty	75 (5.9%)	22 (6.8%)	4 (7.4%)	31 (6.4%)	13 (3.6%)	2 (6.3%)	3 (14.3%)	.22
MPA plasty	171 (13.4%)	17 (5.3%)	4 (7.4%)	97 (19.9%)	47 (13.0%)	3 (9.4%)	3 (14.3%)	**<.001**
TV procedure	176 (13.8%)	68 (21.1%)	5 (9.3%)	47 (9.6%)	47 (13.0%)	2 (6.3%)	7 (33.3%)	**<.001**
RVOT procedure	156 (12.2%)	8 (2.5%)	14 (25.9%)	102 (20.9%)	28 (7.8%)	4 (12.5%)	0 (0%)	**<.001**
RV resection	48 (3.8%)	18 (5.6%)	5 (9.3%)	11 (2.3%)	13 (3.6%)	0 (0%)	1 (4.8%)	**.04**
VSD closure	59 (4.6%)	13 (4.0%)	1 (1.9%)	25 (5.1%)	19 (5.3%)	1 (3.1%)	0 (0%)	.70
PDA ligation	5 (0.4%)	0 (0%)	1 (1.9%)	2 (0.4%)	1 (0.3%)	1 (3.1%)	0 (0%)	.06
ASD/PFO closure	284 (22.2%)	123 (38.2%)	9 (16.7%)	52 (10.7%)	92 (25.5%)	4 (12.5%)	4 (19.0%)	**<.001**
Aortic valve procedure	25 (2.0%)	15 (4.7%)	0 (0%)	5 (1.0%)	5 (1.4%)	0 (0%)	0 (0%)	**.004**
AVR	9 (0.7%)	0 (0%)	1 (1.9%)	5 (1.0%)	2 (0.6%)	1 (3.1%)	0 (0%)	.22
Mitral valve procedure	20 (1.6%)	8 (2.5%)	1 (1.9%)	7 (1.4%)	3 (0.8%)	1 (3.1%)	0 (0%)	.56
LVOTO procedure	7 (0.5%)	5 (1.6%)	1 (1.9%)	1 (0.2%)	0 (0%)	0 (0%)	0 (0%)	.05
Epicardial PM	36 (2.8%)	10 (3.1%)	3 (5.6%)	11 (2.3%)	12 (3.3%)	0 (0%)	0 (0%)	.55
Other	301 (23.6%)	74 (23.0%)	17 (31.5%)	114 (23.4%)	80 (22.2%)	8 (25.0%)	8 (38.1%)	.44
On anticoagulation at discharge	859 (67.2%)	307 (95.3%)	33 (61.1%)	210 (43.0%)	273 (75.6%)	21 (65.6%)	15 (71.4%)	**<.001**
Anticoagulation								**<.001**
Aspirin alone	746 (58.4%)	280 (87.0%)	27 (50.0%)	163 (33.4%)	244 (67.6%)	18 (56.3%)	14 (66.7%)	
Coumadin alone	51 (4.0%)	6 (1.9%)	4 (7.4%)	29 (5.9%)	9 (2.5%)	3 (9.4%)	0 (0%)	
Aspirin/coumadin	24 (1.9%)	6 (1.9%)	2 (3.7%)	5 (1.0%)	11 (3.0%)	0 (0%)	0 (0%)	
Other	38 (3.0%)	15 (4.7%)	0 (0%)	13 (2.7%)	9 (2.5%)	0 (0%)	1 (4.8%)	
None	419 (32.8%)	15 (4.7%)	21 (38.9%)	278 (57.0%)	88 (24.4%)	11 (34.4%)	6 (28.6%)	
LOS, d	1275	322	54	486	360	32	21	
Median (IQR)	6 (5, 7)	6 (5, 7)	6 (5, 7)	5 (4, 7)	6 (5, 7)	7 (5, 10)	6 (5, 13)	**<.001**
LOS tertile								**<.001**
T1 ≤ 5	548 (43.0%)	106 (32.9%)	24 (44.4%)	247 (50.8%)	153 (42.5%)	10 (31.3%)	8 (38.1%)	
T2 6-7 d	443 (34.7%)	147 (45.7%)	18 (33.3%)	134 (27.6%)	132 (36.7%)	9 (28.1%)	3 (14.3%)	
T3 >7 d	284 (22.3%)	69 (21.4%)	12 (22.2%)	105 (21.6%)	75 (20.8%)	13 (40.6%)	10 (47.6%)	

(Continued)

TABLE 1. Continued

Variables	Overall	Sorin Mitroflow	St Jude	CE PERIMOUNT	CE Magna/ Magna Ease	Hancock	Other	*P*
Predischarge echocardiogram								
Pulmonary regurgitation								**<.001**
None	414 (41.4%)	81 (27.2%)	31 (81.6%)	157 (49.8%)	108 (35.8%)	29 (96.7%)	8 (47.1%)	
Trivial	357 (35.7%)	147 (49.3%)	4 (10.5%)	88 (27.9%)	109 (36.1%)	1 (3.3%)	8 (47.1%)	
Mild	210 (21.0%)	67 (22.5%)	3 (7.9%)	61 (19.4%)	79 (26.2%)	0 (0%)	0 (0%)	
Mild-moderate	1 (0.1%)	1 (0.3%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	
Moderate	12 (1.2%)	2 (0.7%)	0 (0%)	7 (2.2%)	3 (1.0%)	0 (0%)	0 (0%)	
Moderate-severe	2 (0.2%)	0 (0%)	0 (0%)	1 (0.3%)	1 (0.3%)	0 (0%)	0 (0%)	
Severe	4 (0.4%)	0 (0%)	0 (0%)	1 (0.3%)	2 (0.7%)	0 (0%)	1 (5.9%)	
Paravalvular leak	17 (1.8%)	5 (1.7%)	0 (0%)	8 (2.9%)	4 (1.3%)	0 (0%)	0 (0%)	.56
Pulmonary stenosis								**<.001**
None	630 (63.4%)	156 (52.3%)	20 (52.6%)	210 (70.0%)	199 (64.0%)	29 (96.7%)	16 (94.1%)	
Trivial	128 (12.9%)	63 (21.1%)	3 (7.9%)	17 (5.7%)	45 (14.5%)	0 (0%)	0 (0%)	
Mild	216 (21.7%)	76 (25.5%)	12 (31.6%)	63 (21.0%)	63 (20.3%)	1 (3.3%)	1 (5.9%)	
Mild-moderate	10 (1.0%)	3 (1.0%)	2 (5.3%)	4 (1.3%)	1 (0.3%)	0 (0%)	0 (0%)	
Moderate	8 (0.8%)	0 (0%)	1 (2.6%)	5 (1.7%)	2 (0.6%)	0 (0%)	0 (0%)	
Moderate-severe	0	–	–	–	–	–	–	
Severe	2 (0.2%)	0 (0%)	0 (0%)	1 (0.3%)	1 (0.3%)	0 (0%)	0 (0%)	
RV dysfunction								**<.001**
None	601 (56.8%)	141 (47.2%)	29 (74.4%)	221 (63.0%)	173 (53.6%)	27 (90.0%)	10 (58.8%)	
Trivial	62 (5.9%)	25 (8.4%)	1 (2.6%)	20 (5.7%)	16 (5.0%)	0 (0%)	0 (0%)	
Mild	236 (22.3%)	98 (32.8%)	4 (10.3%)	52 (14.8%)	76 (23.5%)	2 (6.7%)	4 (23.5%)	
Mild-moderate	38 (3.6%)	9 (3.0%)	1 (2.6%)	12 (3.4%)	15 (4.6%)	0 (0%)	1 (5.9%)	
Moderate	92 (8.7%)	21 (7.0%)	2 (5.1%)	34 (9.7%)	32 (9.9%)	1 (3.3%)	2 (11.8%)	
Moderate-severe	9 (0.8%)	2 (0.7%)	0 (0%)	4 (1.1%)	3 (0.9%)	0 (0%)	0 (0%)	
Severe	21 (2.0%)	3 (1.0%)	2 (5.1%)	8 (2.3%)	8 (2.5%)	0 (0%)	0 (0%)	
LV dysfunction								.29
None	936 (87.3%)	252 (83.2%)	37 (94.9%)	326 (91.1%)	278 (85.5%)	27 (90.0%)	16 (94.1%)	
Trivial	47 (4.4%)	21 (6.9%)	0 (0%)	10 (2.8%)	16 (4.9%)	0 (0%)	0 (0%)	
Mild	62 (5.8%)	24 (7.9%)	2 (5.1%)	10 (2.8%)	24 (7.4%)	2 (6.7%)	0 (0%)	
Mild-moderate	5 (0.5%)	1 (0.3%)	0 (0%)	2 (0.6%)	2 (0.6%)	0 (0%)	0 (0%)	
Moderate	15 (1.4%)	3 (1.0%)	0 (0%)	5 (1.4%)	5 (1.5%)	1 (3.3%)	1 (5.9%)	
Moderate-severe	1 (0.1%)	0 (0%)	0 (0%)	1 (0.3%)	0 (0%)	0 (0%)	0 (0%)	
Severe	6 (0.6%)	2 (0.7%)	0 (0%)	4 (1.1%)	0 (0%)	0 (0%)	0 (0%)	
Last follow-up echocardiogram								
N	1134	310	38	397	339	30	20	
Age at echo, y	20.8	20.4	16.8	21.2	22.1	18.3	14.3	**<.001**
Median (IQR)	(15.1, 29.0)	(14.4, 26.4)	(11.2, 20.0)	(15.5, 30.6)	(16.3, 31.6)	(15.3, 22.9)	(5.3, 27.8)	
Paravalvular leak	10 (0.9%)	4 (1.3%)	0 (0%)	6 (1.8%)	0 (0%)	0 (0%)	0 (0%)	.23
Pulmonary regurgitation								**.008**
None	328 (30.1%)	93 (30.1%)	17 (47.2%)	116 (31.4%)	79 (24.0%)	17 (58.6%)	6 (35.3%)	
Trivial	291 (26.7%)	98 (31.7%)	7 (19.4%)	89 (24.1%)	87 (26.4%)	4 (13.8%)	6 (35.3%)	
Mild	324 (29.8%)	87 (28.2%)	6 (16.7%)	108 (29.3%)	114 (34.7%)	5 (17.2%)	4 (23.5%)	
Mild-moderate	35 (3.2%)	6 (1.9%)	1 (2.8%)	13 (3.5%)	12 (3.6%)	2 (6.9%)	1 (5.9%)	
Moderate	88 (8.1%)	15 (4.9%)	4 (11.1%)	37 (10.0%)	31 (9.4%)	1 (3.4%)	0 (0%)	
Moderate-severe	8 (0.7%)	6 (1.9%)	0 (0%)	1 (0.3%)	1 (0.3%)	0 (0%)	0 (0%)	
Severe	15 (1.4%)	4 (1.3%)	1 (2.8%)	5 (1.4%)	5 (1.5%)	0 (0%)	0 (0%)	
Pulmonary stenosis								**<.001**
None	408 (38.2%)	81 (26.2%)	10 (28.6%)	149 (43.3%)	151 (45.2%)	11 (37.9%)	6 (33.3%)	
Trivial	162 (15.2%)	63 (20.4%)	2 (5.7%)	39 (11.3%)	52 (15.6%)	3 (10.3%)	3 (16.7%)	
Mild	405 (37.9%)	134 (43.4%)	21 (60.0%)	121 (35.2%)	109 (32.6%)	12 (41.4%)	8 (44.4%)	
Mild-moderate	27 (2.5%)	11 (3.6%)	0 (0%)	9 (2.6%)	6 (1.8%)	0 (0%)	1 (5.6%)	
Moderate	62 (5.8%)	19 (6.1%)	2 (5.7%)	26 (7.6%)	12 (3.6%)	3 (10.3%)	0 (0%)	

(Continued)

TABLE 1. Continued

Variables	Overall	Sorin Mitroflow	St Jude	CE PERIMOUNT	CE Magna/ Magna Ease	Hancock	Other	*P*
Moderate-severe	5 (0.5%)	1 (0.3%)	0 (0%)	0 (0%)	4 (1.2%)	0 (0%)	0 (0%)	
Severe	0	–	–	–	–	–	–	
RV dysfunction								**.008**
None	726 (64.4%)	194 (62.6%)	29 (80.6%)	262 (66.0%)	201 (59.8%)	25 (83.3%)	15 (83.3%)	
Trivial	72 (6.4%)	23 (7.4%)	2 (5.6%)	29 (7.3%)	18 (5.4%)	0 (0%)	0 (0%)	
Mild	224 (19.9%)	72 (23.2%)	4 (11.1%)	62 (15.6%)	81 (24.1%)	4 (13.3%)	1 (5.6%)	
Mild-moderate	21 (1.9%)	3 (1.0%)	0 (0%)	9 (2.3%)	7 (2.1%)	1 (3.3%)	1 (5.6%)	
Moderate	53 (4.7%)	16 (5.2%)	1 (2.8%)	15 (3.8%)	21 (6.3%)	0 (0%)	0 (0%)	
Moderate-severe	6 (0.5%)	0 (0%)	0 (0%)	6 (1.5%)	0 (0%)	0 (0%)	0 (0%)	
Severe	25 (2.2%)	2 (0.6%)	0 (0%)	14 (3.5%)	8 (2.4%)	0 (0%)	1 (5.6%)	
LV dysfunction								.88
None	971 (86.2%)	266 (85.8%)	35 (94.6%)	345 (87.6%)	282 (83.7%)	26 (86.7%)	17 (94.4%)	
Trivial	57 (5.1%)	19 (6.1%)	1 (2.7%)	19 (4.8%)	17 (5.0%)	0 (0%)	1 (5.6%)	
Mild	65 (5.8%)	20 (6.5%)	1 (2.7%)	17 (4.3%)	24 (7.1%)	3 (10.0%)	0 (0%)	
Mild-moderate	7 (0.6%)	1 (0.3%)	0 (0%)	3 (0.8%)	3 (0.9%)	0 (0%)	0 (0%)	
Moderate	14 (1.2%)	2 (0.6%)	0 (0%)	4 (1.0%)	7 (2.1%)	1 (3.3%)	0 (0%)	
Moderate-severe	1 (0.1%)	1 (0.3%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	
Severe	11 (1.0%)	1 (0.3%)	0 (0%)	6 (1.5%)	4 (1.2%)	0 (0%)	0 (0%)	

Bold indicates statistically significant *P* values. *CE*, Carpentier-Edwards; *SD*, standard deviation; *IQR*, interquartile range; *BSA*, body surface area; *TOF*, tetralogy of Fallot; *PA*, pulmonary atresia; *CAVC*, complete atrioventricular canal; *PV*, pulmonary valve; *dTGA*, dextro-Transposition of the great arteries; *PVR*, pulmonary valve replacement; *RVOT/TP*, right ventricular outflow tract/transannular patch; *PR/PS*, pulmonary regurgitation/pulmonary stenosis; *LPA*, left pulmonary artery; *RPA*, right pulmonary artery; *MPA*, main pulmonary artery; *TV*, tricuspid valve; *RVOT*, right ventricular outflow tract; *RV*, right ventricular; *VSD*, ventricular septal defect; *PDA*, patent ductus arteriosus; *ASD/PFO*, atrial septal defect/patent foramen ovale; *AVR*, aortic valve replacement; *LVOTO*, left ventricular outflow tract obstruction; *PM*, pacemaker; *LOS*, length of stay; *LV*, left ventricular.

Patients receiving a Hancock valve were younger (median, 7.8 years) than those who received the St Jude (14.3 years), CE Magna/Magna Ease (17.5 years), CE PERIMOUNT valves (16.8 years), and Mitroflow valves (16.4 years).

The Sorin Mitroflow (100%), St Jude (94%), and CE Magna/Magna Ease (62%) valves were implanted in patients in 2008 or later, in contrast to Hancock valves that were primarily (97%) implanted in patients before 2008. The CE PERIMOUNT valves were equally distributed before and after 2008.

PR was the most common indication for PVR (64%) and its prevalence differed by valve type, being least common (38%) for Hancock valves ($P < .001$). An indication of PS was 11% and was most common for cases with Hancock valves (53%), greater than the prevalence in patients with the other 4 valve types (7.5%-11.5%; $P < .001$). Combined PS and PR was the indication in 19% of cases.

The type of outflow tract left at the original primary operation was most commonly a transannular patch (67%), homograft (12%) or native outflow tract (11%). At the index PVR operation, an augmented right ventricular outflow tract was used for the majority of cases (71% overall).

Anticoagulation was used in 67% of patients at discharge, with the majority on aspirin only (58%). The median hospital length of stay was 6 days (IQR, 5-7 days). Overall mean follow-up was 4.57 ± 3.72 years (Table 2).

Reintervention Rates

One-hundred-fifty-nine (12%) underwent a surgical (n = 53) or cardiac catheterization (n = 83) PVR or for PV balloon dilation only (n = 23). The overall median time to reintervention was 13.0 years (IQR, 8.0-15.9 years). The overall unadjusted 1-, 3-, and 5-year Kaplan–Meier estimated reintervention rates were 1%, 3%, and 8%, respectively (Figure 2, *A*).

Reintervention Rates by Age

Time to reintervention differed significantly by age at surgery ($P < .001$; Table 2 and Figure 3, *A*). The median time to reintervention in patients <18 years of age was 11.4 years (IQR, 6.1-15.9 years) and in patients ≥18 years of age was 17.7 years (25th percentile, 13.0. years). The risk of reintervention was approximately 5 times (19% vs 4%) greater for patients <18 years old (hazard ratio [HR], 4.57; 95% confidence interval [CI], 3.02-6.93). Older age at repair in the pediatric cohort was protective against reintervention (HR, 0.87 per year; 95% CI, 0.85-0.89). Among patients who underwent PVR at ≥18 years old, there was no association between age and reintervention.

Reintervention Rates by Valve Type

Median follow-up time was 3.9 years (IQR, 1.2-6.35) and differed by valve type, with a median follow-up of 3.9 years for the Sorin Mitroflow and CE Magna/Magna Ease,

TABLE 2. Overall follow-up and by valve type

Variables	Overall	Sorin Mitroflow	St Jude	CE PERIMOUNT	CE Magna/ Magna Ease	Hancock	Other	*P*
N	1278	322	54	488	361	32	21	
Death	31 (2.4%)	3 (0.9%)	0 (0%)	18 (3.7%)	6 (1.7%)	3 (9.4%)	1 (4.8%)	.008
Follow-up time, y	4.57 ± 3.72	3.98 ± 2.15	2.87 ± 2.12	4.78 ± 4.35	4.46 ± 3.47	9.74 ± 4.75	7.10 ± 4.55	<.001
Median (IQR)	4.05 (1.32, 6.98)	4.26 (2.63, 5.67)	3.17 (0.71, 4.56)	3.90 (0.82, 7.99)	3.97 (1.08, 7.61)	11.69 (8.21, 13.01)	6.67 (3.54, 10.02)	<.001
Follow-up time among deaths, y	3.92 ± 4.07	2.11 ± 3.64	NA	3.50 ± 4.32	3.54 ± 2.38	6.04 ± 3.00	12.76 ± 0.0	.168
Median (IQR)	2.93 (0.39, 7.01)	0.02 (0.01, 6.31)	NA	1.13 (0.21, 7.53)	3.75 (1.21, 4.85)	6.91 (2.69, 8.50)	12.76	.232
Follow-up time among survivors, y	4.58 ± 3.71	3.99 ± 2.14	2.87 ± 2.12	4.83 ± 4.34	4.47 ± 3.48	10.13 ± 4.76	6.81 ± 4.47	<.001
Median (IQR)	4.08 (1.36, 6.98)	4.28 (2.64, 5.67)	3.17 (0.71, 4.56)	4.01 (0.93, 7.99)	3.97 (1.07, 7.63)	11.95 (10.17, 13.26)	6.09 (3.12, 9.41)	<.001

CE, Carpentier-Edwards; *IQR*, interquartile range; *NA*, not applicable.

2.97 years for the St Jude and 8.79 years for the Hancock valves.

The unadjusted 5-year Kaplan–Meier estimated reintervention rates were 24%, 15%, 12%, 4%, and 3% for St Jude, Sorin Mitroflow, Hancock, Magna/Magna Ease, and CE PERIMOUNT valves, respectively. The 3-year reintervention rates for the St Jude, Sorin Mitroflow, and Magna/Magna Ease valves were 8%, 6%, and 2% (0% for Hancock) (Table 3). Figure 2, *B*, shows estimated freedom from reintervention by valve type. The Sorin Mitroflow valve has a greater hazard of reintervention compared with the CE PERIMOUNT, CE Magna/Magna

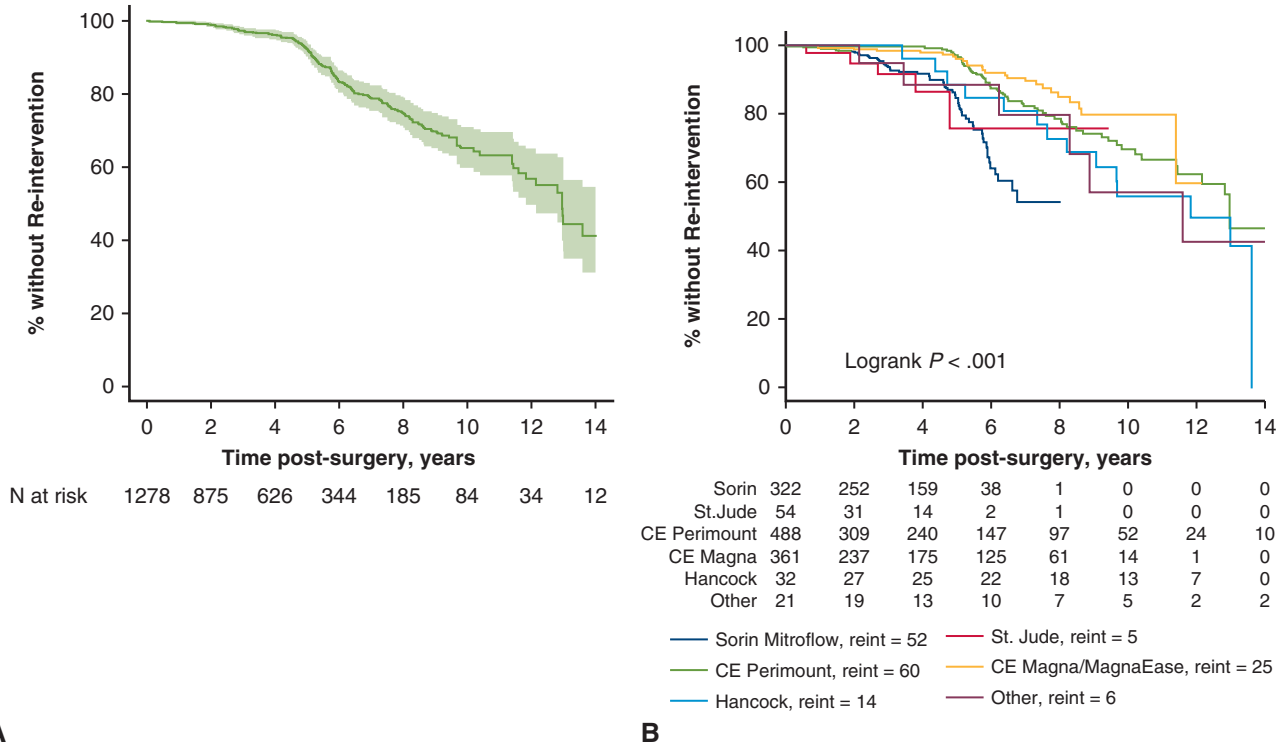
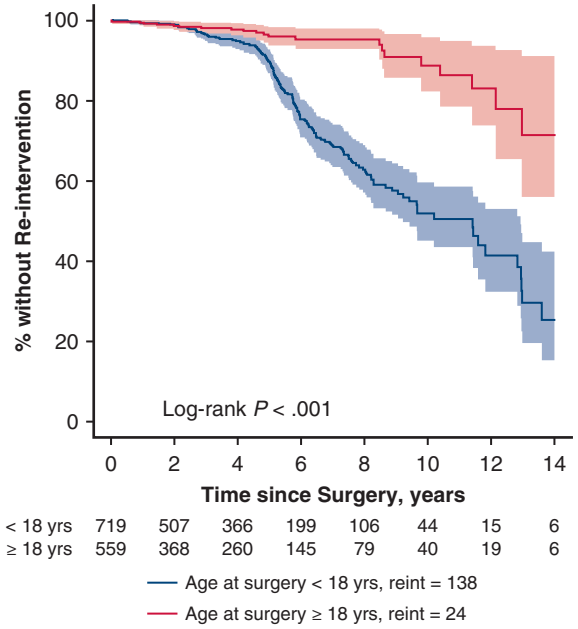
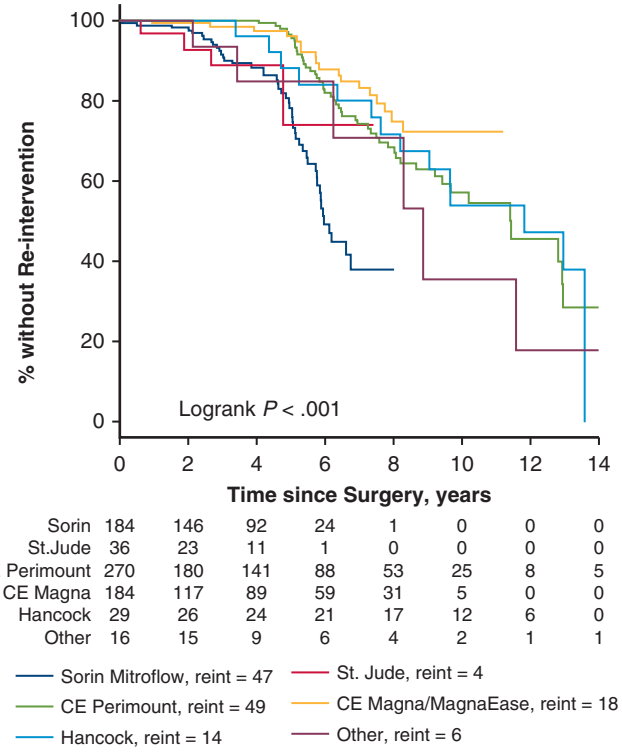
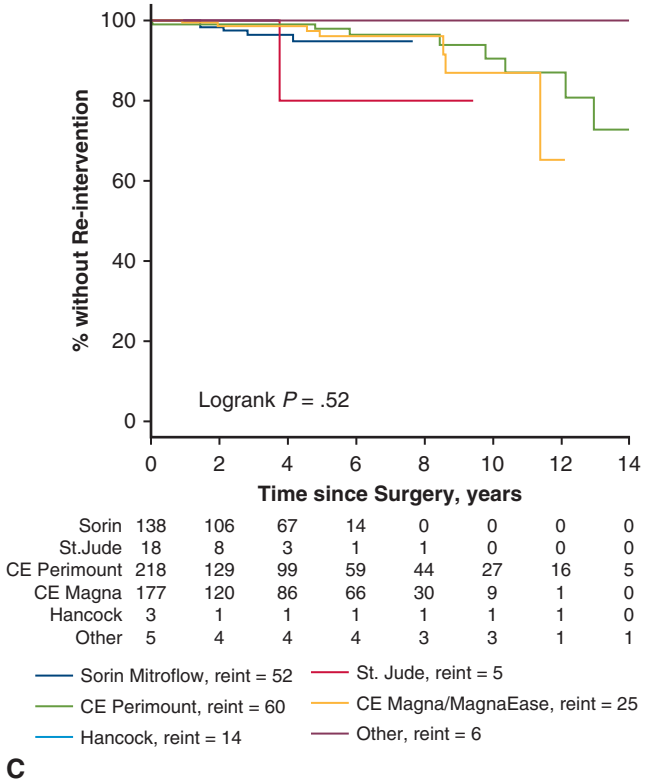


FIGURE 2. A and B, Estimated freedom from reintervention, overall and by valve type. The 5-year freedom from reintervention rate is 92% (95% CI, 90%-94%). Figures are truncated at 14 years. Three events occurred after 14 years, all with a CE PERIMOUNT valve. *Shaded area* denotes pointwise 95% confidence bands. 95% confidence limits for the groups in B are provided in Table E1. *CE*, Carpentier-Edwards.





A



B

C

FIGURE 3. A-C, Estimated freedom from reintervention by age group and by valve type within age group. Child is defined as <18 years; adult is defined as ≥18 years. The 5-year freedom from reintervention rate is 90% (95% CI, 86%-92%) for the <18-year group and 96% (95% CI, 93%-98%) for the ≥18-year group. Figures are truncated at 14 years. Three events occurred after 14 years, all with a CE PERIMOUNT valve; 1 surgery was performed at age <18 years and 2 were performed at ≥18 years. *Shaded area* denotes pointwise 95% confidence bands. 95% confidence limits for the groups in B and C are provided in Tables E2 and E3, respectively. *CE*, Carpentier-Edwards.

Ease, and Hancock valves. The St Jude valve has a greater hazard of reintervention compared with both CE valves. The CE Magna/Magna Ease and the CE PERIMOUNT valves have a similar time to reintervention. The Hancock has a greater hazard of reintervention compared with CE Magna/Magna Ease valves. The "other" valve type group has similar times to reintervention compared with all types of valves. ($P < .001$).

Because younger age is so strongly related to reintervention as well as to valve type, 85% of cases with reintervention occurred among the patients who underwent surgery at <18 years old, who comprised 56% of the cohort. Figure 3 displays the estimated probability of freedom from reintervention by age group; estimates are also provided by valve type within age group, to limit the confounding effects of age when examining differences by valve type.

Other Univariate Risk Factors for Reintervention

Measures related to younger patient age at surgery were risk factors for reintervention (ie, lower BSA; $P < .001$) (Table 4). Larger labeled valve size (HR, 0.80 per millimeter) and smaller valve size/BSA (HR, 0.93 per millimeter decrease), were protective against reintervention ($P < .001$). Surgical indication of PR alone is associated with a lower risk of reintervention than the other indications ($P < .001$), whereas the presence of both PR and PS is significantly associated with greater risk of reintervention ($P < .001$). An additional procedure (of any type) concurrent with the index PVR was not a risk factor for reintervention; however, 4 individual procedures were related to a greater reintervention risk: left and main pulmonary artery plasty, RV resection, and atrial septal defect/patent foramen ovale closure. Placement of an epicardial pacemaker

TABLE 3. Reintervention overall and by valve type

Variable	Overall	Sorin Mitroflow	St. Jude	CE PERIMOUNT	CE Magna/Magna Ease	Hancock	Other	*P*
N	1278	322	54	488	361	32	21	
Reintervention	162 (12.7%)	52 (16.1%)	5 (9.3%)	60 (12.3%)	25 (6.9%)	14 (43.8%)	6 (28.6%)	**<.001**
Follow-up time, y								
Median (IQR)	3.91 (1.20, 6.35)	3.92 (2.19, 5.27)	2.97 (0.65, 4.31)	3.78 (0.65, 6.88)	3.93 (1.01, 7.32)	8.79 (4.54, 11.89)	5.16 (2.69, 8.88)	**<.001**
Reintervention reason								.12
PR	44 (27.5%)	11 (22.0%)	1 (20.0%)	20 (33.3%)	10 (40.0%)	0 (0%)	2 (33.3%)	
PS/RVOTO	110 (68.8%)	36 (72.0%)	3 (60.0%)	39 (65.0%)	14 (56.0%)	14 (100%)	4 (66.7%)	
SBE	6 (3.8%)	3 (6.0%)	1 (20.0%)	1 (1.7%)	1 (4.0%)	0 (0%)	0 (0%)	
Unknown	2	2	0	0	0	0	0	
Reintervention type								**.01**
Balloon dilation	23 (14.5%)	5 (9.6%)	0 (0%)	10 (17.2%)	2 (8.3%)	5 (35.7%)	1 (16.7%)	
Balloon dilation and MV placement	83 (52.2%)	37 (71.2%)	3 (60.0%)	25 (43.1%)	14 (58.3%)	1 (7.1%)	3 (50.0%)	
PVR	53 (33.3%)	10 (19.2%)	2 (40.0%)	23 (39.7%)	8 (33.3%)	8 (57.1%)	2 (33.3%)	
Unknown	3	0	0	2	1	0	0	
Freedom from reintervention (95% CI)								<.001
1-y event rate	0.99 (0.99, 1.00)	0.99 (0.97-1.00)	0.98 (0.85-1.00)	1.00 (0.98-1.00)	0.99 (0.97-1.00)	1.00 (1.00-1.00)	1.00 (1.00-1.00)	
3-y event rate	0.97 (0.96, 0.98)	0.94 (0.90-0.96)	0.92 (0.76-0.97)	1.00 (0.98-1.00)	0.98 (0.96-0.99)	1.00 (1.00-1.00)	0.95 (0.68-0.99)	
5-y event rate	0.92 (0.90, 0.94)	0.85 (0.78-0.89)	0.76 (0.44-0.91)	0.97 (0.94-0.98)	0.96 (0.92-0.98)	0.88 (0.68-0.96)	0.88 (0.61-0.97)	
10-y event rate	0.65 (0.59, 0.70)	0.54 (0.41-0.65)	0.76 (0.44-0.91)	0.70 (0.61-0.77)	0.80 (0.70-0.87)	0.56 (0.34-0.73)	0.57 (0.23-0.80)	
Time to reintervention percentiles								
25% tile	8.0	5.7	NA	8.7	11.4	7.6	8.3	
50% tile (median)	13.0	NA	NA	13.0	NA	11.8	11.6	
75% tile	15.9	NA	NA	17.7	NA	13.6	NA	

Bold indicates statistically significant *P* values. *CE*, Carpentier-Edwards; *IQR*, interquartile range; *PR*, pulmonary regurgitation; *PS/RVOTO*, pulmonary stenosis/right ventricular outflow tract obstruction; *SBE*, subacute bacterial endocarditis; *MV*, Melody valve; *PVR*, pulmonary valve replacement; *CI*, confidence interval; *NA*, not available.

TABLE 4. Univariate Cox regression modeling of time to reintervention, adjusted for center variation

Variables	N	Reintervention		HR (95% CI)	*P* value
		Yes (n = 162)	No (n = 1116)		
Valve type					**<.001**
Sorin Mitroflow	322	52 (16.1%)	270 (83.9%)	4.85 (3.39-6.94)	
St. Jude	54	5 (9.3%)	49 (90.7%)	5.04 (1.56-16.28)	
CE PERIMOUNT	488	60 (12.3%)	428 (87.7%)	1.42 (0.98-2.07)	
CE Magna/Magna Ease	361	25 (6.9%)	336 (93.1%)	Ref	
Hancock	32	14 (43.8%)	18 (56.3%)	2.02 (1.47-2.78)	
Other	21	6 (28.6%)	15 (71.4%)	2.07 (1.15-3.75)	
Sex					.373
Female	647	82 (12.7%)	565 (87.3%)	0.91 (0.74-1.12)	
Male	630	79 (12.5%)	551 (87.5%)	Ref	
Age at surgery, y		10.93 ± 9.71	20.53 ± 12.75		
Age group					**<.001**
Child <18 y	719	138 (19.2%)	581 (80.8%)	4.57 (3.02-6.93)	
Adult ≥18 y	559	24 (4.3%)	535 (95.7%)	Ref	
Age at surgery, piecewise term					**<.001**
Child <18 y				0.87 (0.85-0.89)	
Adult ≥18 y				0.97 (0.94-1.01)	
BSA, m^2		1.07 ± 0.52	1.54 ± 0.47	0.84 (0.81-0.88) Per 0.1-unit ↑	**<.001**
Fundamental diagnosis					.248
TOF	839	113 (13.5%)	726 (86.5%)	1.12 (0.92-1.36)	
Other	400	47 (11.8%)	353 (88.3%)	Ref	
Previous PVR					.359
Yes	165	21 (12.7%)	144 (87.3%)	0.84 (0.49-1.47)	
No	1113	141 (12.7%)	972 (87.3%)	Ref	
Non-native outflow tract					**<.001**
Yes	983	148 (15.1%)	835 (84.9%)	1.45 (1.23-1.70)	
No	122	9 (7.4%)	113 (92.6%)	Ref	
Surgical indication (s)					
Pulmonary regurgitation					**.009**
Yes	822	85 (10.3%)	737 (89.7%)	0.58 (0.39-0.87)	
No	456	77 (16.9%)	379 (83.1%)	Ref	
Pulmonary stenosis					.496
Yes	144	24 (16.7%)	120 (83.3%)	0.86 (0.55-1.34)	
No	1134	138 (12.2%)	996 (87.8%)	Ref	
PR/PS					**<.001**
Yes	239	43 (18.0%)	196 (82.0%)	2.22 (1.46-3.37)	
No	1039	119 (11.5%)	920 (88.5%)	Ref	
Endocarditis					NA
Yes	9	0 (0%)	9 (100%)		
No	1269	162 (12.8%)	1107 (87.2%)		
Other					**<.001**
Yes	158	25 (15.8%)	133 (84.2%)	1.43 (1.17-1.76)	
No	1120	137 (12.2%)	983 (87.8%)	Ref	
Was PVR primary indication for surgery					.120
Yes	1157	147 (12.7%)	1010 (87.3%)	0.71 (0.46-1.09)	
No	120	15 (12.5%)	105 (87.5%)	Ref	
Valve size, mm		22.56 ± 3.59	25.31 ± 2.60	0.80 (0.74-0.86)	**<.001**
Valve size/BSA		25.23 ± 9.92	18.36 ± 6.90	1.08 (1.07-1.08)	**<.001**

(Continued)

TABLE 4. Continued

Variables	N	Reintervention		HR (95% CI)	*P* value
		Yes (n = 162)	No (n = 1116)		
Valve-insertion method					**.002**
1: Isolated with PA closure	183	15 (8.2%)	168 (91.8%)	Ref	
2: Anterior patch	908	115 (12.7%)	793 (87.3%)	1.32 (0.63-2.74)	
3: Dacron/HEMASHIELD tube	129	25 (19.4%)	104 (80.6%)	1.49 (0.76-2.89)	
4: Gore-Tex tube	43	6 (14.0%)	37 (86.0%)	1.09 (0.42-2.84)	
5: Other	13	1 (7.7%)	12 (92.3%)	2.20 (0.18-27.56)	
Combined procedures					.124
Yes	353	48 (13.6%)	305 (86.4%)	0.86 (0.71-1.04)	
No	925	114 (12.3%)	811 (87.7%)	Ref	
LPA plasty					**.022**
Yes	125	27 (21.6%)	98 (78.4%)	1.60 (1.07-2.41)	
No	1153	135 (11.7%)	1018 (88.3%)	Ref	
RPA plasty					.063
Yes	75	18 (24.0%)	57 (76.0%)	1.94 (0.97-3.90)	
No	1203	144 (12.0%)	1059 (88.0%)	Ref	
MPA plasty					**.048**
Yes	171	20 (11.7%)	151 (88.3%)	1.32 (1.00-1.74)	
No	1107	142 (12.8%)	965 (87.2%)	Ref	
TV procedure					.111
Yes	176	18 (10.2%)	158 (89.8%)	0.72 (0.48-1.08)	
No	1102	144 (13.1%)	958 (86.9%)	Ref	
RVOT procedure					.695
Yes	156	17 (10.9%)	139 (89.1%)	1.15 (0.58-2.26)	
No	1122	145 (12.9%)	977 (87.1%)	Ref	
RV resection					**<.001**
Yes	48	9 (18.8%)	39 (81.3%)	1.33 (1.22-1.45)	
No	1230	153 (12.4%)	1077 (87.6%)	Ref	
VSD closure					.220
Yes	59	9 (15.3%)	50 (84.7%)	0.86 (0.68-1.09)	
No	1219	153 (12.6%)	1066 (87.4%)	Ref	
PDA ligation					.667
Yes	5	1 (20.0%)	4 (80.0%)	1.10 (0.72-1.68)	
No	1273	161 (12.6%)	1112 (87.4%)	Ref	
ASD/PFO closure					**.026**
Yes	284	40 (14.1%)	244 (85.9%)	1.54 (1.05-2.24)	
No	994	122 (12.3%)	872 (87.7%)	Ref	
Aortic valve procedure					.264
Yes	25	3 (12.0%)	22 (88.0%)	1.22 (0.86-1.75)	
No	1253	159 (12.7%)	1094 (87.3%)	Ref	
AVR					.485
Yes	9	2 (22.2%)	7 (77.8%)	1.62 (0.42-6.20)	
No	1269	160 (12.6%)	1109 (87.4%)	Ref	
MV procedure					.486
Yes	20	3 (15.0%)	17 (85.0%)	1.30 (0.62-2.74)	
No	1258	159 (12.6%)	1099 (87.4%)	Ref	
LVOTO procedure					NA
Yes	7	0 (0%)	7 (100%)		
No	1271	162 (12.7%)	1109 (87.3%)		
Epicardial PM					**.007**
Yes	36	1 (2.8%)	35 (97.2%)	0.15 (0.04-0.60)	
No	1242	161 (13.0%)	1081 (87.0%)	Ref	

(Continued)

TABLE 4. Continued

Variables	N	Reintervention		HR (95% CI)	*P* value
		Yes (n = 162)	No (n = 1116)		
Other					.555
Yes	301	37 (12.3%)	264 (87.7%)	1.08 (0.84-1.39)	
No	977	125 (12.8%)	852 (87.2%)	Ref	
Anticoagulation					**<.001**
Aspirin alone	746	108 (14.5%)	638 (85.5%)	0.97 (0.83-1.12)	
Coumadin alone	51	6 (11.8%)	45 (88.2%)	0.33 (0.17-0.64)	
Aspirin/Coumadin	24	2 (8.3%)	22 (91.7%)	0.27 (0.23-0.32)	
Other	38	1 (2.6%)	37 (97.4%)	0.69 (0.41-1.16)	
None	419	45 (10.7%)	374 (89.3%)	Ref	
Predischarge echocardiogram					
At least mild PR					**.004**
Yes	229	32 (14.0%)	197 (86.0%)	1.30 (1.09-1.55)	
No	771	102 (13.2%)	669 (86.8%)	Ref	
At least mild PS					.511
Yes	236	27 (11.4%)	209 (88.6%)	1.06 (0.89-1.28)	
No	758	109 (14.4%)	649 (85.6%)	Ref	
Paravalvular leak					.100
Yes	17	3 (17.6%)	14 (82.4%)	3.02 (0.81-11.25)	
No	936	130 (13.9%)	806 (86.1%)	Ref	
At least mild RV dysfunction					**<.001**
Yes	396	55 (13.9%)	341 (86.1%)	1.25 (1.11-1.41)	
No	663	85 (12.8%)	578 (87.2%)	Ref	
At least mild LV dysfunction					.716
Yes	89	14 (15.7%)	75 (84.3%)	1.06 (0.77-1.47)	
No	983	128 (13.0%)	855 (87.0%)	Ref	

Bold indicates statistically significant *P* values. *HR*, Hazard ratio; *CI*, confidence interval; *CE*, Carpentier-Edwards; *BSA*, body surface area; *TOF*, tetralogy of Fallot; *PVR*, pulmonary valve replacement; *PR*, pulmonary regurgitation; *PS*, pulmonary stenosis; *NA*, not available; *PA*, pulmonary atresia; *LPA*, left pulmonary artery; *RPA*, right pulmonary artery; *MPA*, main pulmonary artery; *TV*, tricuspid valve; *RVOT*, right ventricular outflow tract; *RV*, right ventricular; *VSD*, ventricular septal defect; *PDA*, patent ductus arteriosus; *ASD/PFO*, atrial septal defect/patent foramen ovale; *AVR*, aortic valve replacement; *MV*, Melody valve; *LVOTO*, left ventricular outflow tract obstruction; *PM*, pacemaker; *LV*, left ventricular.

concurrent with the index PVR was protective against reintervention ($P = .007$). A known paravalvular leak at discharge was not associated with an increased rate of reintervention. Anticoagulation strategies of Coumadin alone and a Coumadin/aspirin combination are both associated with a lower rate of reintervention compared with no anticoagulation therapy ($P < .001$).

Multivariable Model for Time to Reintervention

It was of interest to examine the association of fundamental diagnosis and reintervention after accounting for differences in age. The 210 patients with PA underwent surgery at a younger age than other patients (median 13.0 vs 17.1 years, $P < .001$). In crude analysis, PA was a risk factor for reintervention (HR, 1.54; 95% CI, 1.31-1.80, $P < .001$). After we accounted for age, the association was weaker: the age-adjusted HR for PA versus all other patients was 1.12 (95% CI, 1.001-1.25, $P = .045$). We also explored the reintervention risk for those with a native versus non-native outflow tract. Patients with a native outflow tract were significantly older at time of original PVR (median 17.8 vs 15.8 years, $P = .02$). These patients were at increased risk of reintervention, independent of age (age-adjusted HR, 0.79; 95% CI, 0.72-0.87, $P < .001$).

To address the question of valve oversizing, we analyzed valve size indexed to BSA, which was a significant univariate risk factor for reintervention in patients younger than 18 years but not in adults (interaction $P = .005$). In those younger than 18 years, the HR was 1.06 (95% CI, 1.05-1.07); in older patients, the HR was 0.91 (95% CI, 0.82-1.01).

A multivariable model was constructed to examine covariate-adjusted differences in time to reintervention by valve type. All variables (excluding echo parameters) with a *P* value <.20 in the univariate analysis were included as candidates. Table 5 shows that the Sorin Mitroflow and St Jude valves have similar time to reintervention and greater covariate-adjusted hazard of reintervention than the Hancock and CE Magna/Magna Ease valves; the Sorin Mitroflow also has a greater covariate-adjusted hazard ratio relative to the CE PERIMOUNT. The HRs are smaller than in the univariate analysis in Table 4, due to accounting for differences in age and valve size. Other factors that are independently associated with a greater hazard of

reintervention are the lack of a concomitant tricuspid valve procedure, younger age (among pediatric age only), and smaller valve size. In patients younger than 18 years of age, the hazard of reintervention is 76% greater with each younger year of age at PVR. In adults, there is no association between age and time to reintervention. As a sensitivity analysis, we also constructed the multivariable model with the smaller sample size resulting from inclusion of the predischarge echo parameters as candidates during model selection. The final model included the same 4 factors shown in Table 5.

DISCUSSION

PVR has become increasingly common as survival for patients with CHD has improved and indications for PVR have evolved.[8,9] Symptoms and functional status improve following PVR, and there is a reduction in PR and tricuspid regurgitation, RV size, and dysfunction.[10,11] Historically, pulmonary and aortic homografts were used but have been shown to develop early failure,[4] leading to reintervention. This was particularly problematic for younger patients and is suspected to be immune-related.[12,13] Therefore, other valve types for PVR have been considered including stent-mounted Melody transcatheter valves,[14,15] mechanical valves,[16,17] bovine jugular Contegra,[18,19] and most commonly, stented bioprosthetic valves.[20]

TABLE 5. Multivariable Cox regression model of time to reintervention, adjusted for center variation (n = 1278, no. with reintervention = 162, pseudo R^2 = 0.14)

Variable	HR (95% CI)	*P* value
Valve type		**<.001**
Sorin vs St Jude	1.02 (0.39-2.67)	
Sorin vs CE PERIMOUNT	3.23 (2.17-4.81)	
Sorin vs CE Magna/Magna Ease	3.49 (2.44-4.99)	
Sorin vs Hancock	10.56 (7.75-14.37)	
Sorin vs other	1.93 (1.37-2.71)	
St Jude vs CE PERIMOUNT	3.18 (0.95-10.61)	
St Jude vs CE Magna/Magna Ease	3.43 (1.05-11.22)	
St Jude vs Hancock	10.40 (3.33-32.47)	
St Jude vs other	1.90 (0.66-5.47)	
CE PERIMOUNT vs Magna/Magna Ease	1.08 (0.81-1.43)	
CE PERIMOUNT vs Hancock	3.27 (2.94-3.64)	
CE PERIMOUNT vs other	0.60 (0.47-0.76)	
CE Magna/Magna Ease vs Hancock	3.02 (2.41-3.82)	
CE Magna/Magna Ease vs other	0.55 (0.40-0.76)	
Hancock vs other	0.18 (0.15-0.22)	
Age at surgery		**<.001**
<18 y	0.93 (0.89-0.97)	.002
≥18 y	0.98 (0.94-1.01)	.146
Valve size, mm	0.85 (0.81-0.90)	**<.001**
Combined procedure (tricuspid valve)	0.66 (0.47-0.93)	**.019**

Bold indicates statistically significant *P* values. *HR*, Hazard ratio; *CI*, confidence interval; *CE*, Carpentier-Edwards.

We previously reported a large single-center experience of 611 patients undergoing bioprosthetic PVR between 1996 and 2014 where children were shown to have more than a 5-fold greater reintervention rate than adults independent of age and valve type.[7]

In this large multicenter series of children and young adults undergoing bioprosthetic PVR at 8 different centers, we sought to confirm our previously reported single-center experience. Herein, we report early and mid-term outcomes with reintervention differences based on patient age and valve type.

Single-center series have also reported a number of additional risk factors associated with PV reintervention following bioprosthetic PVR. These include fundamental diagnosis,[4,21] an indication of PS for surgery,[21] male sex,[3,21] variables associated with age,[3,4,6,21,22] large valve size at implantation (ie, z score > 2.0),[22,23] valve type,[7,23] previous PVR, and smaller normalized valve size.[3]

The fundamental diagnosis was identified as a risk factor for reoperation in several single center series. It has been speculated that RV to pulmonary artery conduits implanted in the nonorthotopic position have an increased amount of turbulence and are predisposed to early failure.[4] In our series, we found an increased age-adjusted risk of reintervention for the 210 patients with pulmonary atresia compared with other patients. We also found a lower hazard of reintervention with the use of the native outflow tract.

A surgical indication of PS at the time of PVR has also been reported as a significant factor for reoperation.[21] Similarly, we found PS as a risk factor for reintervention. In addition, we found that combined PR and PS incurred a 2-fold risk of early reintervention whereas isolated PR was associated with a lower risk of reintervention. In neither historical reports nor our analysis was the indication for reoperation associated with PS an independent predictor of outcome, suggesting that reoperation was likely correlated with age, valve size, or choice of valve type.

Male sex was identified as a risk factor for reintervention in earlier single-center reports.[3,21] However, we found no association between sex and the hazard of reintervention. It is possible that age distributions by sex differed in earlier reports, with male patients having a younger mean age.

Reoperation following PVR is more common in younger patients.[3,4,6,7] In our univariate analysis, previous PVR was not predictive for reintervention. However, in both our single-center[7] and multicenter experiences, we similarly found that measures related to younger patient age at surgery were risk factors for reintervention, whereas larger labeled valve size and smaller valve size for BSA were protective against reintervention. In our series, the median time to reintervention in patients less than (vs greater than or equal to) 18 years of age was 11.4 versus 17.7 years. The risk of reintervention was approximately 5 times greater (19% vs 4%) for younger patients, with a 7% lower hazard for

reintervention for each year of age. We found no association between age and reintervention in older patients.

Subclinical leaflet thrombosis has been shown in adults to occur frequently in bioprosthetic aortic valves leading to increased rates of strokes and likely early valve failure. Anticoagulation with both novel oral anticoagulants and warfarin, but not dual platelet therapy, has been shown to be effective in prevention or treatment of the thrombosis.[24,25] Interestingly, in this series anticoagulation strategies of Coumadin ± aspirin are both associated with a lower rate of reintervention compared with no anticoagulation therapy. It is likely that reduced leaflet motion from thrombus following PVR leads to early valve failure.

Failing surgically implanted bioprosthetic valves demonstrate leaflet calcification, thickness and immobility leading to PS or PR.[26,27] Bioprosthetic heart valves without anti-mineralization treatment have been shown to be at significantly greater risk for more rapid failure in both the aortic[5] and pulmonary[7] positions. Younger[5] and older patients undergoing aortic valve replacement with the Sorin Mitroflow LXA pericardial valve showed more rapid progression of aortic stenosis requiring reintervention.[5,27-29] In younger patients, no leaflets were torn or otherwise disrupted, the calcification process did not involve host cells and the leaflets were not associated with inflammation or infection.[5] In our series, after controlling for both valve size and patient age, the hazard of PV reintervention when an untreated Mitroflow LXA valve was implanted remained 3- to 9-fold greater than the hazards associated with the other valve types and seems likely related to the similar mechanisms previously reported.

However, in addition to anti-mineralization treatment, there appear to be other potentially important factors associated with structural valve failure such as stent type, stent-leaflet interface, flow characteristics, associated endocarditis,[30,31] and/or hematologic factors. The CE PERIMOUNT valve was a second-generation valve where low pressure fixation techniques were used and was first introduced clinically in 1981. It was tri-leaflet valve consisting of bovine pericardial leaflets mounted underneath a flexible cobalt-chromium stent and did not have anti-mineralization treatments applied.[32,33] The third-generation Magna/Magna Ease valves were first implanted in 2005 and had a Thermafix treatment applied to help mitigate the effects of calcification.[34] Possibly the strongest comparison in this multicenter series are the second-generation CE PERIMOUNT valves versus the third-generation–treated Magna/Magna Ease valves. Combined, they accounted for 67% of all PVRs in the series, all centers implanted, and implants were distributed over the study period. Despite the differences in fixation and tissue treatment, they had similar covariate-adjusted distributions of times to reintervention (hazard ratio of 1.1).

The majority (>95%) of patients in this series had stented bovine pericardial valves implanted which limited our ability to determine differences between other commonly used stented or non-stented ("freestyle" porcine aortic root[35]) bioprosthetic porcine valves. Most commonly used valves included the Hancock II, PERIMOUNT, Freestyle, and CE porcine valves. Freedom from valve dysfunction/failure was only 20% at 10 years. In our larger cohort, freedom from reintervention at 10 years was much greater, 30% to 44% for these same types of valves.

The strategy of oversizing valves has also been used to try and improve valve longevity; however, this has not been shown to improve outcomes. Karamlou and colleagues[36] found that placing oversized pulmonary homograft conduits in both younger and older patients did not improve freedom from PV failure with conduit failure remaining more frequent in younger patients. Chen and colleagues[22] also showed that bioprosthetic PV oversizing in patients less than 20 years old was a significant predictor of structural valve deterioration. In this series, we found increased risk of reintervention with increasing valve size indexed to BSA, regardless of age. Furthermore, we found that the absence of a concurrent tricuspid valve procedure at the time of PV replacement was an independent risk factor for reintervention.

Study Limitations

First, although these analyses used covariate adjustment, such adjustment may be imperfect to perform direct comparison of those who received the non-treated Sorin Mitroflow LXA and CE PERIMOUNT valves, because the number of patients who overlap with similar ages was relatively small. However, the age-stratified analysis also demonstrated differences in outcome according to valve type. Second, this analysis does not take into account repeated reinterventions on the same patient; we have modeled the time to first reintervention. There were 165 cases who had more than 1 reintervention during the period of follow-up and if included may yield slightly greater statistical power to detect significant risk factors. Third, 30 patients without a reintervention status in the dataset were censored at their initial surgery discharge date. Fourth, a large number of comparisons were performed, and some may be significant due to chance. Fifth, the pairwise comparisons of valve types shown in Tables 3 and 4 are not formally adjusted (ie, use of a smaller significance level) for multiple comparisons. Sixth, predischarge echocardiograms are not available for all patients. However, none of the effect sizes in univariate analysis were clinically significant, regardless of P value, other than perhaps paravalvular leak. Furthermore, a sensitivity analysis restricted to the cohort with echocardiograms did not identify any echocardiographic measures as independent predictors of reintervention. Seventh, our median follow-up was 4.1 years, with 25% having over 7 years of follow-up; however, with longer follow-up, some of the clinically significant associations that we report may have been statistically significantly. Last, because the period of follow-up for this

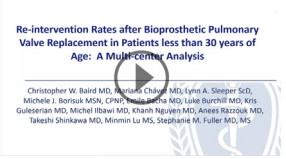
analysis spanned approximately 3 decades, it is possible that aspects of surgical technique and threshold for reintervention have changed and are not accounted for in our comparisons.

CONCLUSIONS

In this large, multicenter study with more than one half the cohort being pediatric patients, bioprosthetic PVR in patients with CHD has acceptable short-term outcomes, with only 8% requiring reintervention within 5 years. Smaller valve sizes and younger age in those younger than 18 years old are independent predictors of a shorter time to reintervention. There were no age-related differences in reintervention in adults. Different valve types also have different rates of reintervention. Independent of patient age at surgery and valve size, the Sorin Mitroflow and St Jude valves have a more rapid rate of reintervention compared to the CE PERIMOUNT and Magna/Magna Ease valves, which have similar distribution of time to reintervention.

Webcast

You can watch a Webcast of this AATS meeting presentation by going to: https://aats.blob.core.windows.net/media/19%20AM/Monday_May6/202BD/202BD/S75%20-%20Right%20ventricular%20outflow%20reconstruction/S75_2.mp4.



Conflict of Interest Statement

The authors reported no conflicts of interest.

The *Journal* policy requires editors and reviewers to disclose conflicts of interest and to decline handling or reviewing manuscripts for which they may have a conflict of interest. The editors and reviewers of this article have no conflicts of interest.

References

1. Baskett RJ, Ross DB, Nanton MA, Murphy DA. Factors in the early failure of cryopreserved homograft pulmonary valves in children: preserved immunogenicity? *J Thorac Cardiovasc Surg*. 1996;112:1170-9.
2. Shinkawa T, Anagnostopoulos PV, Johnson NC, Watanabe N, Sapru A, Azakie A. Performance of bovine pericardial valves in the pulmonary position. *Ann Thorac Surg*. 2010;90:1295-300.
3. Caldarone CA, McCrindle BW, Van Arsdell GS, Coles JG, Webb G, Freedom RM, et al. Independent factors associated with longevity of prosthetic pulmonary valves and valved conduits. *J Thorac Cardiovasc Surg*. 2000;120:1022-31.
4. Lee C, Park CS, Lee CH, Kwak JG, Kim SJ, Shim WS, et al. Durability of bioprosthetic valves in the pulmonary position: long-term follow-up of 181 implants in patients with congenital heart disease. *J Thorac Cardiovasc Surg*. 2011;142:351-8.
5. Saleeb SF, Newburger JW, Geva T, Baird CW, Gauvreau K, Padera RF, et al. Accelerated degeneration of a bovine pericardial bioprosthetic aortic valve in children and young adults. *Circulation*. 2014;130:51-60.
6. Chen XJ, Smith PB, Jaggers J, Lodge AJ. Bioprosthetic pulmonary valve replacement: contemporary analysis of a large, single-center series of 170 cases. *J Thorac Cardiovasc Surg*. 2013;146:1461-6.
7. Nomoto R, Sleeper LA, Borisuk MJ, Bergerson L, Pigula FA, Emani S, et al. Outcome and performance of bioprosthetic pulmonary valve replacement in patients with congenital heart disease. *J Thorac Cardiovasc Surg*. 2016;152:1333-42.
8. Burchill LJ, Wald RM, Harris L, Colman JM, Silversides CK. Pulmonary valve replacement in adults with repaired tetralogy of Fallot. *Semin Thorac Cardiovasc Surg Pediatr Card Surg Annu*. 2011;14:92-7.
9. Geva T. Indications for pulmonary valve replacement in repaired tetralogy of Fallot: the quest continues. *Circulation*. 2013;128:1855-7.
10. Gengsakul A, Harris L, Bradley TJ, Webb GD, Williams WG, Siu SC, et al. The impact of pulmonary valve replacement after tetralogy of Fallot repair: a matched comparison. *Eur J Cardiothorac Surg*. 2007;32:462-8.
11. Warner KG, O'Brien PK, Rhodes J, Kaur A, Robinson DA, Payne DD. Expanding the indications for pulmonary valve replacement after repair of tetralogy of Fallot. *Ann Thorac Surg*. 2003;76:1066-71.
12. Albert JD, Bishop DA, Fullerton DA, Campbell DN, Clarke DR. Conduit reconstruction of the right ventricular outflow tract: lessons learned in a twelve-year experience. *J Thorac Cardiovasc Surg*. 1993;106:228-36.
13. Rajani B, Mee RB, Ratliff NB. Evidence for rejection of homograft cardiac valves in infants. *J Thorac Cardiovasc Surg*. 1998;115:111-7.
14. Caughron H, Kim D, Kamioka N, Lerakis S, Yousef A, Maini A, et al. Repeat pulmonary valve replacement: similar intermediate-term outcomes with surgical and transcatheter procedures. *JACC Cardiovasc Interv*. 2018;11:2495-503.
15. Cabalka AK, Asnes JD, Balzer DT, Cheatham JP, Gillespie MJ, Jones TK, et al. Transcatheter pulmonary valve replacement using the melody valve for treatment of dysfunctional surgical bioprostheses: a multicenter study. *J Thorac Cardiovasc Surg*. 2018;155:1712-24.
16. Pragt H, van Melle J, Javadikasgari H, Man Seo D, Stulak J, Knez I, et al. Mechanical valves in the pulmonary position: an international retrospective analysis. *J Thorac Cardiovasc Surg*. 2017;154:1368-70.
17. Waterbolk TW, Hoendermis ES, den Hamer IJ, Ebels T. Pulmonary valve replacement with a mechanical prosthesis. Promising results of 28 procedures in patients with congenital heart disease. *Eur J Cardiothorac Surg*. 2006;30:28-32.
18. Shebani SO, McGuirk S, Baghai M, Stickley J, De Giovanni JV, Bulock FA, et al. Right ventricular outflow tract reconstruction using Contegra valved conduit: natural history and conduit performance under pressure. *Eur J Cardiothorac Surg*. 2006;29:397-405.
19. Protopapas AD, Athanasiou T. Contegra conduit for reconstruction of the right ventricular outflow tract: a review of published early and mid-time results. *J Cardiothorac Surg*. 2008;3:62.
20. Ferraz Cavalcanti PE, Sá MP, Santos CA, Esmeraldo IM, de Escobar RR, de Menezes AM, et al. Pulmonary valve replacement after operative repair of tetralogy of Fallot: meta-analysis and meta-regression of 3,118 patients from 48 studies. *J Am Coll Cardiol*. 2013;62:2227-43.
21. Zubairi R, Malik S, Jaquiss RD, Imamura M, Gossett J, Morrow WR. Risk factors for prosthesis failure in pulmonary valve replacement. *Ann Thorac Surg*. 2011;91:561-5.
22. Chen PC, Sager MS, Zurakowski D, Pigula D, Baird CW, Mayer JE, et al. Younger age and valve oversizing are predictors of structural valve deterioration after pulmonary valve replacement in patients with tetralogy of Fallot. *J Thorac Cardiovasc Surg*. 2012;143:352-60.
23. Jang W, Kim YJ, Choi K, Lim H-G, Kim W-H, Lee JR. Mid-term results of bioprosthetic pulmonary valve replacement in pulmonary regurgitation after tetralogy of Fallot repair. *Eur J Cardiothorac Surg*. 2012;42:e1-8.
24. Chakravarty T, Søndergaard, Friedman F, De Backer O, Berman D, Kofoed KF, et al. Subclinical leaflet thrombosis in surgical and transcatheter bioprosthetic aortic valves: an observational study. *Lancet*. 2017;389:2383-92.
25. Makkar RR, Fontana G, Jilaihawi H, Chakravarty T, Kofoed KF, De Backer O, et al. Possible subclinical leaflet thrombosis in bioprosthetic aortic valves. *N Engl J Med*. 2015;373:2015-24.
26. Callahan R, Bergersen L, Baird CW, Porras D, Esch J, Lock JE, et al. Mechanism of valve failure and efficacy of reintervention through catheterization in patients with bioprosthetic valves in the pulmonary position. *Ann Pediatr Cardiol*. 2017;10:11-7.
27. Butany J, Feng T, Luk A, Law K, Suri R, Nair V. Modes of failure in explanted Mitroflow pericardial valves. *Ann Thorac Surg*. 2011;92:1621-7.
28. Alvarez JR, Sierra J, Vega M, Adrio B, Martinez-Comendado J, Gude F, et al. Early calcification of the aortic Mitroflow pericardial bioprosthesis in the elderly. *Interact Cardiovasc Thorac Surg*. 2009;5:842-6.

29. Pomar JL, Jamieson WR, Pelletier LC, Gerein AN, Castellá M, Brownlee RT. Mitroflow pericardial bioprosthesis: clinical performance to ten years. *Ann Thorac Surg*. 1995;60:S305-9.
30. Mery CM, Guzman-Pruneda FA, De Leon LE, Zhang W, Terwelp MD, Bocchini CE, et al. Risk factors for development of endocarditis and reintervention in patients undergoing right ventricle to pulmonary artery valved conduit placement. *J Thorac Cardiovasc Surg*. 2016;151:432-9.
31. Mery CM, Fraser CD. Why do some conduits get infected and others don't? *J Thorac Cardiovasc Surg*. 2018;155:333-4.
32. Bourguignon T, Bouquiaux-Stablo AL, Candolfi P, Mirza A, Loardi C, May M, et al. Very long-term outcomes of the Carpentier-Edwards Perimount valve in aortic position. *Ann Thorac Surg*. 2015;99:831-7.
33. Edwards Lifesciences. Carpentier-Edwards PERIMOUNT Pericardial Bioprosthesis Model 2700 Aortic [brochure]. Irvine, Calif: Edwards Lifesciences; 2008.
34. Edwards Lifesciences. Carpentier-Edwards PERIMOUNT Magna Ease Pericardial Aortic Bioprosthesis Model 3300TFX [brochure]. Irvine, Calif: Edwards Lifesciences; 2009.
35. Kanter KR, Fyfe DA, Mahle WT, Forbess JM, Kirshbom PM. Results with the Freestyle porcine aortic root for right ventricular outflow tract reconstruction in children. *Ann Thorac Surg*. 2003;76:1889-95.
36. Karamlou T, Ungerleider RM, Alsoufi B, Burch G, Silberbach M, Reller M, et al. Oversizing pulmonary homograft conduits does not significantly de-crease allograft failure in children. *Eur J Cardiothorac Surg*. 2005;27:548-53.

Key Words: pulmonary valve, bioprosthesis, heart defects, congenital, pulmonary regurgitation, pulmonary stenosis, reoperation, pediatric

Discussion

Presenter: Dr Mariana Chavez

Dr James A. Quintessenza *(Lexington, Ky)*. Congratulations on an excellent, clear presentation with a lot of data. I appreciate receiving the manuscript in advance. This report is on twelve hundred seventy-eight patients younger than the age of 30 years undergoing pulmonary valve replacement. It's a multicenter retrospective review, and it's consistent with other reports in the literature.

We saw in the performance of these valves that all bioprostheses will degenerate over time, and more so in younger patients. The performance of the Sorin, the Mitroflow, and the St Jude valve seem to be worse. In addition, the second-generation PERIMOUNT and the third-generation Magna valves were not much different, suggesting that we haven't made a lot of progress in terms of preventing degeneration in these newer valves. The overall take-home message, I think, is that we still have a lot of work to do regarding durability for our patients.

My interventional colleagues tell me that transcatheter valves and stents don't seem to degenerate. There may be some improvement with those types of transcatheter approaches, and I think time will tell us. Possibly, newer biomaterials, synthetic materials such as expanded polytetrafluoroethylene or newer mechanical valves coupled with improved methods to modulate the coagulation system will provide some better outcomes as well.

We will see, but for now, we have what we have. I just have a few questions really to clarify some of the points you made. In the multivariable analysis, both younger age as well as small valve size were independent risk factors for early degeneration. Can we assume that it wasn't just smaller valves in younger children that simply failed due to outgrowth, but there is something else operative in the interaction of these valves in younger patients, which leads to more rapid decline?

Dr Mariana Chavez *(Boston, Mass)*. Thank you for your question. We didn't look at other variables such as genetics or any other thing that could influence the reintervention, but we do take into account that smaller patients eventually outgrow their valves. So that's why we need to replace it. All these valves were not necessarily replaced because they failed, but because the patient outgrew them, so it is important for us to take into account that these children have congenital heart disease and they may have associated diseases.

We didn't look into other factors specifically for genetic diseases or concomitant disease.

Dr Quintessenza. In previous reports, longevity of right ventricular outflow tract reconstruction using the native outflow tract seemed to be an advantage and you didn't find that in this analysis. Do you think that difference might be due to the use of homographs versus heterografts, in terms of creating extra-anatomic versus native outflow tracks? We might ask Chris to help you.

Dr Christopher W. Baird *(Boston, Mass)*. So it sounds like the question is: the angle of the valve and the way the valve sits in either the native outflow tract or extra-anatomic, is there a difference in this study? We didn't show any difference. However, based on our experience, we've seen that in patients with pulmonary atresia where their valves tend to fail quicker. I think we weren't able to tease that out in this study. So I don't think we can really address that.

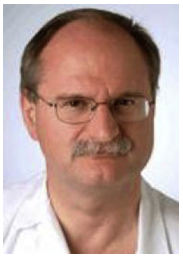
Dr Quintessenza. One more question: In the manuscript, larger valve sizes and a smaller valve size to body surface area protects against earlier intervention. That seems to imply that putting in a bigger valve is good up to a certain point, but if you oversize, you start going in the other direction. Do you have an optimal valve size to body surface area or z value that you would recommend for valve implantation?

Dr Baird. That is a difficult question. As everyone knows, every valve has a different external diameter in relation to its internal diameter. So, the problem becomes when you break down each individual valve and you compare the external and internal diameters, they're different. So you have to take a ratio of those—and every valve was different. Thus,

in a study that has multiple valve sizes and multiple types, it's difficult. The ideal valve size out of all these valves was like a 23, among all patients, but that's hard to extrapolate.

Dr John W. Brown *(Indianapolis, Ind)*. Enjoyed this study. Is the takeaway message that porcine valves in the pulmonary position are more durable than pericardial valves in the pulmonary position? I just tried to look at the graphs; it seemed to me that the porcine valves were lasting longer. Is that a misinterpretation of the data?

Dr Baird. I don't think it's a misinterpretation of the data. The problem is that there was a limited number of porcine valves in the entire series. So I think our sense is: yes, porcine valves did better in younger patients, but it was skewed toward porcine valves going in younger patients.



Dr Antonio F. Corno *(Leicester, United Kingdom)*. It seems that the malfunctioning of the valve implanted in the pulmonary position is due mostly to platelet deposition on the leaflets. Were the patients in your study treated with antiplatelet treatment in all the centers, and for how long? Thank you.

Dr Chavez. We did not take into account how long the patient was on antiplatelets, but we did record if they were on aspirin, on Coumadin, or a combination, and in our univariate analysis; there was no significant risk to being only on aspirin or a combination.

Dr Damien J. LaPar *(New York, NY)*. Great presentation. Regarding the question of porcine and pericardial valves, as congenital surgeons, we are at the mercy of industry. We are using valves created for aortic valve disease in adults for pulmonary valve replacement. And porcine valves versus pericardial valves—pericardial valves actually have a greater opening pressure. It's negligible; it's like 4 mm of mercury versus 2 mm of mercury. For that reason, I don't know if that has an impact on longevity, but I think it's a little tough to tease out your conclusion that pericardial valves are superior to porcine valves. Is that a pretty solid finding?

Dr Baird. That is a very important point but that wasn't one of our ultimate conclusions. It was a finding of the data we had. The problem is that we had a limited number of porcine valves, and they were in primarily younger patients. I think what we can say is: based on this data set, porcine valves were better in younger patients. So we can't make that general statement among older patients because we didn't have very many porcine valves in older patients.

Dr LaPar. Just one question to add: Did the porcine valves in the younger patients have Hancock conduits?

Dr Baird. Yes, a portion of them.

Unidentified speaker. Chris, that study shows what we all know, and the cardiologists are telling us, that in the first 5 years, the bioprosthetic valves are going to do well, then they'll start failing, and then after 8 to 13 years you'll need to do a reintervention. And I was taught never to put a homograft, except that decellularized homograft in other conditions in the Ross operation, for example, now can last 15 to 20 years, and they'll have an easier transcatheter valve insertion. So, do you think we should change what we were all taught and never put homographs in the native outflow, because you can put them in the annulus of the pulmonary valve and put on the patch, and leave them in an anatomic position. So do you think this is the message?

Dr Baird. Let's just take a poll of hands in the room, since Carl's here. I'm not sure that's true. How many folks put homographs in the pulmonary position to replace the pulmonary valve? So not everyone puts bioprosthetic, and certainly if Tom Spray was here—I think he used to put homographs in the pulmonary valve position in older patients. So I don't think we can jump to that conclusion, but this study certainly does not address that.

Unidentified speaker. I'm a valve engineer, so this comes from a valve designer standpoint. We all know that every valve design is different. My first question is: Does all this reintervention stem primarily from structural valve deterioration? Second, are all the failure modes the same? As compared with a standard valve, failure in a porcine valve may be more due to calcification and the pericardial valve may be more due to pannus ingrowth.

Dr Chavez. For your first question, not all of the reinterventions were due to valve failure. Some were due to the patients outgrowing their valve. Dr Baird will take the second question.

Dr Baird. We can't answer that question adequately with this study. This study is a large multicenter study and looked at reintervention. It didn't look at mechanism of failure. But what we can tell is it the patients who failed had predominantly pulmonary stenosis going into the valve replacement. I think a really important point that wasn't brought up here was the anticoagulation strategy. I think that's really fundamental, and I think folks are doing things very differently with regards to that now.

Our current anticoagulation strategy is aspirin and Coumadin for 3 months, but you may want to comment on your strategy.

Dr Corno. What we are seeing (we use only porcine valve) is the reduction of the leaflets' movements due to platelet deposition. That's why I previously asked how long in your study the aspirin had been given. We give aspirin always for 3 months now; should we move to a much longer period if it's true and proven that it is platelet deposition reducing the leaflets' movement?

TABLE E1. Pointwise 95% confidence limits for freedom from reintervention, by valve type, overall cohort (see Figure 2, *B*)

Years since surgery	Freedom from reintervention (95% CI)					
	Sorin Mitroflow	St Jude	CE PERIMOUNT	CE Magna/Magna Ease	Hancock	Other
3	0.94 (0.90-0.96)	0.92 (0.76-0.97)	1.00 (0.98-1.00)	0.98 (0.96-0.99)	1.00 (1.00-1.00)	0.95 (0.68-0.99)
6	0.64 (0.54-0.73)	0.76 (0.44-0.91)	0.87 (0.82-0.91)	0.92 (0.87-0.95)	0.85 (0.64-0.94)	0.88 (0.61-0.97)
9	0.54 (0.41-0.65)	0.76 (0.44-0.91)	0.74 (0.66-0.80)	0.80 (0.70-0.87)	0.69 (0.47-0.83)	0.57 (0.23-0.80)
12	0.54 (0.41-0.65)	0.76 (0.44-0.91)	0.62 (0.52-0.71)	0.60 (0.21-0.84)	0.50 (0.28-0.68)	0.43 (0.12-0.71)

CI, Confidence interval; *CE*, Carpentier-Edwards.

TABLE E2. Pointwise 95% confidence limits for freedom from reintervention, by valve type, pediatric cohort (see Figure 3, *B*)

Years since surgery	Freedom from reintervention (95% CI)					
	Sorin Mitroflow	St Jude	CE PERIMOUNT	CE Magna/Magna Ease	Hancock	Other
3	0.92 (0.86-0.95)	0.89 (0.69-0.96)	1.00 (1.00-1.00)	0.98 (0.94-1.00)	1.00 (1.00-1.00)	0.93 (0.61-0.99)
6	0.49 (0.37-0.60)	0.74 (0.34-0.92)	0.82 (0.74-0.88)	0.88 (0.78-0.93)	0.84 (0.63-0.94)	0.85 (0.51-0.96)
9	0.38 (0.24-0.51)	0.74 (0.34-0.92)	0.63 (0.52-0.72)	0.72 (0.58-0.82)	0.67 (0.45-0.82)	0.35 (0.05-0.69)
12	0.38 (0.24-0.51)	0.74 (0.34-0.92)	0.46 (0.30-0.60)	0.72 (0.58-0.82)	0.47 (0.25-0.66)	0.18 (0.01-0.53)

CI, Confidence interval; *CE*, Carpentier-Edwards.

TABLE E3. Pointwise 95% confidence limits for freedom from reintervention, by valve type, adult cohort (see Figure 3, *C*)

Years since surgery	Freedom from reintervention (95% CI)					
	Sorin Mitroflow	St Jude	CE PERIMOUNT	CE Magna/Magna Ease	Hancock	Other
3	0.96 (0.90-0.99)	1.00 (1.00-1.00)	0.99 (0.96-1.00)	0.98 (0.94-1.00)	1.00 (1.00-1.00)	1.00 (1.00-1.00)
6	0.95 (0.87-0.98)	0.80 (0.20-0.97)	0.96 (0.89-0.99)	0.96 (0.89-0.99)	1.00 (1.00-1.00)	1.00 (1.00-1.00)
9	0.95 (0.87-0.98)	0.80 (0.20-0.97)	0.94 (0.84-0.98)	0.87 (0.67-0.95)	1.00 (1.00-1.00)	1.00 (1.00-1.00)
12	0.95 (0.87-0.98)	0.80 (0.20-0.97)	0.87 (0.71-0.94)	0.65 (0.19-0.90)	1.00 (1.00-1.00)	1.00 (1.00-1.00)

CI, Confidence interval; *CE*, Carpentier-Edwards.