Congenital aortic and truncal valve reconstruction using the Ozaki technique: Short-term clinical results

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ABSTRACT

Objectives: Aortic valve reconstruction (AVRec) with neocuspidization or the Ozaki procedure with complete cusp replacement for aortic valve disease has excellent mid-term results in adults. Limited results of AVRec in pediatric patients have been reported. We report our early outcomes of the Ozaki procedure for congenital aortic and truncal valve disease.

Methods: A retrospective analysis was performed on all 57 patients with congenital aortic and truncal valve disease who had a 3-leaflet Ozaki procedure at a single institution from August 2015 to February 2019. Outcome measures included mortality, surgical or catheter-based reinterventions, and echocardiographic measurements.

Results: Twenty-four patients had aortic regurgitation (AR), 6 had aortic stenosis (AS), and 27 patients had AS/AR. Two patients had quadricuspid valves, 26 had tricuspid, 20 had bicuspid, and 9 had unicusp aortic valves. Four patients had truncus arteriosus. Thirty-four patients had previous aortic valve repairs and 5 had replacements. Preoperative echocardiography mean annular diameter was 20.90 ± 4.98 cm and peak gradient for patients with AS/AR was 53.62 ± 22.20 mm Hg. Autologous, Photofix, and CardioCel bovine pericardia were used in 20, 35, and 2 patients. Eight patients required aortic root enlargement and 20 had sinus enlargement. Fifty-one patients had concomitant procedures. Median intensive care unit and hospital length of stay were 1.87 and 6.38 days. There were no hospital mortalities or early conversions to valve replacement. At discharge, 98% of patients had mild or less regurgitation and peak aortic gradient was 16.9 ± 9.5 mm Hg. Two patients underwent aortic valve replacement. At median follow-up of 8.1 months, 96% and 91% of patients had less than moderate regurgitation and stenosis, respectively.

Conclusions: The AVRec procedure has acceptable short-term results and should be considered for valve reconstruction in pediatric patients with congenital aortic and truncal valve disease. Longer-term follow-up is necessary to determine the optimal patch material and late valve function and continued annular growth. (J Thorac Cardiovasc Surg 2021;161:1567-77)

Aortic valve after 3-leaflet Ozaki repair.

CENTRAL MESSAGE

The AVRec or "Ozaki" procedure has excellent short-term results and should be considered for valve reconstruction in patients with congenital aortic and truncal valve disease.

PERSPECTIVE

Surgical outcomes of congenital aortic and truncal valve disease remain problematic. Surgical options are limited due to size limitations, anticoagulation requirements, early calcification, and structural valve deterioration. The AVRec or "Ozaki" procedure has provided an excellent alternative in adult patients, and early results appear promising in children.

See Commentaries on pages 1578, 1579, and 1582.

Improved understanding of aortic valve anatomy and the mechanisms causing aortic valve disease, along with newer reconstructive techniques, have allowed for acceptable early anatomic outcomes following aortic valve repair; however, mid-term results remain problematic. Longer-term success remains limited, with some series suggesting 46% reoperation at 7.5 years in older children.[1] Replacement options with mechanical and bioprosthetic valves are limited due to size, anticoagulation requirements, and a high rate of early calcification and structural valve deterioration. The Ross procedure remains a good option for infants and young children, as it allows for excellent hemodynamics and growth but is limited by the necessity for right ventricular outflow tract reintervention and the increased risk of late autograft insufficiency due to neo-aortic root and ascending aortic dilatation.[2,3] In addition, it is not an option with truncus arteriosus, following arterial switch operation, significant pulmonary valve, or connective tissue diseases.

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Abbreviations and Acronyms

AR	= aortic regurgitation
AS	= aortic stenosis
AVRec	= aortic valve reconstruction
BSA	= body surface area
CI	= confidence interval
CPB	= cardiopulmonary bypass
LVEDV	= left ventricular end diastolic volume
LVEDVz	= z score of the BSA-indexed left ventricular end diastolic volume

Stentless bioprostheses have worked particularly well in older patients with small aortic annuli and have resulted in improved left ventricular function and functional class.[4] Aortic valve reconstruction (AVRec) with neocuspidization functions much like a "stentless" valve.[5] It preserves the natural motion of the aortic annulus during the cardiac cycle and consists of using glutaraldehyde-treated autologous or bovine pericardium to replace 3 aortic valve cusps. It has been applied to a spectrum of aortic valve disease in adults, including those with small annuli, aortic stenosis (AS) and aortic regurgitation (AR), native and prosthetic valve endocarditis, and annulo-aortic ectasia. We report the early outcomes of the AVRec in young patients with congenital aortic and truncal valve disease.

METHODS

From August 2015 to February 2019 neoaortic valve reconstruction of 3 leaflets as described by Ozaki was performed on 57 patients at Boston Children's Hospital (Boston, Mass).[6] Data were retrospectively analyzed from our Ozaki registry following institutional review board approval (IRB-P00026715; approval: December 5, 2017).

Echocardiography

A single reviewer independently measured preoperative, postoperative, discharge, and follow-up echocardiogram images, with a second reviewer analyzing a random sample. Measurements of the aortic valve, root, and ascending aorta were indexed to body surface area (BSA). AS was assessed by peak gradients categorized as follows: none-trivial <15 mm Hg, mild 15 to 25, mild-moderate 26 to 35, moderate 36 to 49, moderate-severe 50 to 59, and severe ≥60 mm Hg. AR was determined by vena contracta and measured in parasternal long-axis views where the diastolic retrograde color flow converged to the narrowest diameter and was indexed to the square root of BSA.[7] AR was estimated as none-trivial if vena contracta indexed to BSA was <2, mild if 2 to 3.9 mm/m^2, moderate if 4 to 6 mm/m^2, and severe if >6 mm/m^2. Leaflet mobility was observed in parasternal long- and short-axis views. One of the limitations was the inability to quantitatively measure leaflet mobility. Options like 3-dimensional echocardiography may allow us to make such measurements in a reliable manner. Coaptation height was measured in diastole from the leaflet tips to the mid-portion where coaptation ended. Left ventricular end-diastolic volume (LVEDV) measurements were taken from reports.

Operative Technique

The technique is shown in Figure 1, *A-E*. All procedures were performed via partial or full sternotomy with cardiopulmonary bypass (CPB). If autologous pericardium was used, it was harvested and tightly attached to the stainless-steel board, adventitia aggressively removed, treated with buffered 0.6% glutaraldehyde solution for 2 or 10 minutes, and then rinsed 3 times in saline for 6 minutes. Due to concerns about stiffened leaflets and concerns for glutaraldehyde-associated calcification, generally after April 2017, the pericardium was fixed for 2 minutes (Table 1). Native cusps were completely excised, removing calcium and/or thick fibrous ridge at the annulus (Figure 1, *A*). Intercommissural edges were then measured using the original sizing device (JOMDD, Tokyo, Japan), providing appropriate tension to reproduce the annulus during diastole, upsizing rather than downsizing if in between sizes (Figure 1, *B*). The new cusps measured size was created from the template (JOMDD) using pericardium (Figure 1, *C*). Autologous, Photofix, and CardioCel bovine pericardia were used in 20, 35, and 2 patient(s), respectively. This technique was previously published.[6] To summarize, the annular margin of the pericardial cusp was sutured with a running 4.0 monofilament suture with a TF needle (Figure 1, *D*). The smooth surface was placed into the left ventricular outflow early in the series, but further consideration was given to concerns about the rough edges of pericardium in the sinus related to the coronaries later in the series. The pericardial cusp was sewn to the top of the commissure using a 3:1 ratio and was designed to have deep coaptation that reaches up to the same horizontal plane as the commissure. The top of the commissure is secured with additional suture and pledget. In patients whom had uni- or bicuspid valves, 3 equal leaflets were created based off the intercoronary commissure. Consideration for performing annular enlargement was given to patients with annular z scores less than 2 and whose native annulus measured less than 15 mm. For patients requiring annular enlargement, Konno and/or Manouguian incisions were made and patched with pericardium (Figure 1, *E*). The sizers were then used to mark the new annulus and the leaflets were sized as previously. To avoid redundant leaflets, the leaflet size must be precisely determined and the sinus and sinotubular junction dimensions cannot be undersized. It is most frequently the noncoronary sinus that is undersized and can be enlarged with pericardium. For patients undergoing ascending aortic reduction, a V-shaped wedge resection of the right lateral aspect of the ascending aorta from crossclamp to sinotubular junction was made, with a goal of reducing the ascending aorta to a z score between 0 and +2 using appropriately sized Hegar dilators as a guide. The ascending aorta was reapproximated with a double layer mattress closure with polypropylene suture.

Anticoagulation

In total, 56 patients were treated with aspirin postoperatively. Beginning November 2017, we generally started patients (n = 25) on coumadin with a goal international normalized ratio of 1.5 to 2.5. One patient received no anticoagulation.

Statistical Analysis

Data are presented as mean ± standard deviation or median and interquartile range. One-sample *t* tests and Wilcoxon signed rank tests was used to test whether changes (eg, preoperative vs discharge, discharge vs last follow-up) echocardiographic z scores differed from zero. Changes over time in echocardiographic parameters were estimated using mixed effects regression modeling. Rates of freedom from reoperation and from at least moderate AR or AS were estimated using Kaplan–Meier methodology. Univariate logistic regression was used to examine associations between leaflet mobility and anticoagulation strategy. Two-sample *t* tests and Fisher exact tests were used to compare continuous and categorical baseline patient factors, respectively, by late AS status and AR status. Statistical significance was defined as a *P* value of .05. Analyses were performed using SAS version 9.4 (SAS Institute, Cary, NC) and R version 3.5.1 (R Foundation for Statistical Computing, Vienna, Austria).

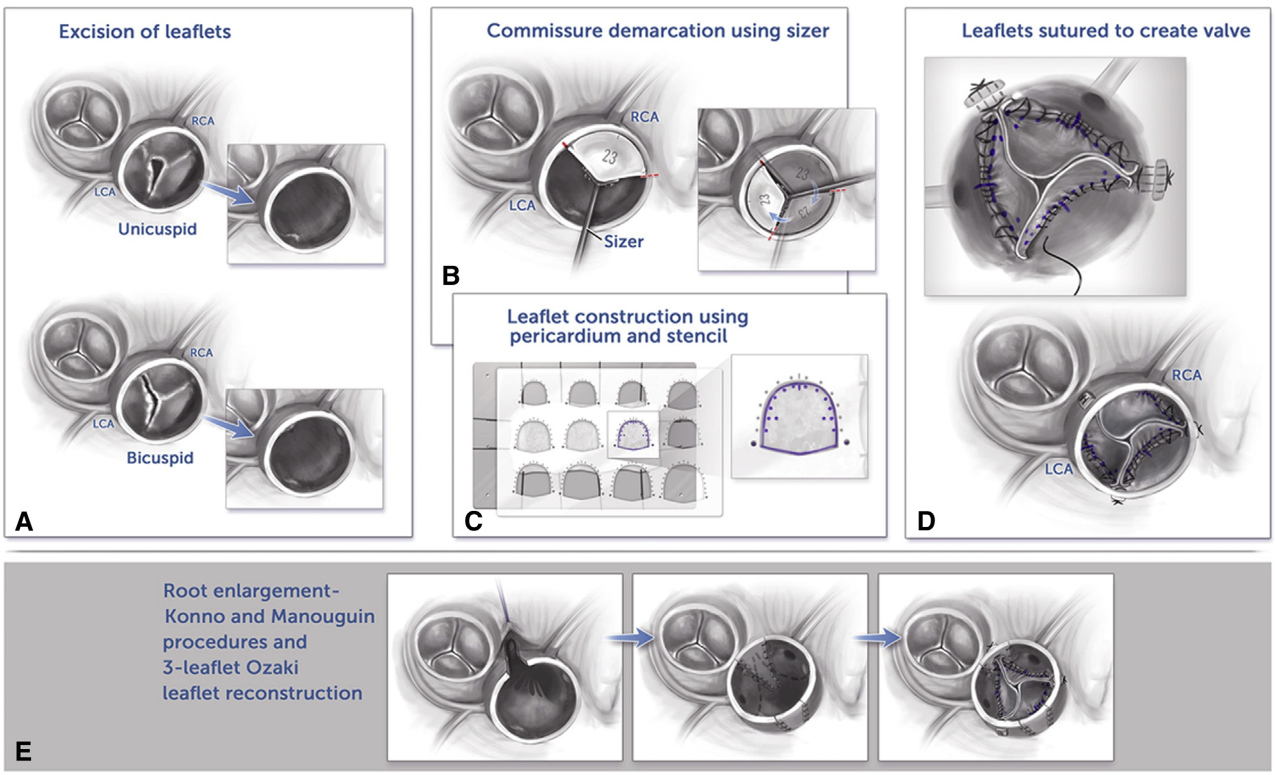

FIGURE 1. AVRec procedure. A, Excision of leaflets. B, Commissure demarcation using sizer. C, Leaflet construction using pericardium and template. D, Leaflets sutured to annulus. E, Aortic root enlargement with Konno and Manouguian procedures. *RCA*, Right coronary artery; *LCA*, left coronary artery.

RESULTS

Demographics

Complete demographic and operative data summarized in Tables 1 and 2. Three leaflets were reconstructed in 57 patients. Twenty-four patients had AR, 6 had AS, and 27 patients had AS/AR. Two patients had quadricuspid, 26 had tricuspid, 20 had bicuspid, and 9 had unicusp aortic valves. Four patients had truncus arteriosus. Thirty-four patients had previous aortic valve repairs, 4 had previous bioprosthetic aortic valve replacements, and 1 had a previous mechanical aortic valve replacement. Five patients had a mini- or partial sternotomy. Eight patients had aortic root enlargements and 20 had sinus enlargements. Concomitant procedures were required in 51 patients, including biventricular repair, mitral valvuloplasty, ascending aortoplasty, aortic root reduction, subaortic membrane resection, and pulmonary artery plasty.

Intraoperative/Early Results

Six patients required reinstitution of CPB. One patient required closure of a gap at the base of the noncoronary leaflet and one required hematoma decompression on the left coronary ostia and all had mild or less aortic insufficiency after revision. Other indications for reinstitution CPB included reduction of redundant leaflets in 3 patients and 1 had a mitral valve replacement. One patient left the operating room with more than mild aortic insufficiency. Median intensive care unit and hospital length of stay were 1.9 and 6.4 days. There were no hospital mortalities, early conversions to valve replacement, or significant hospital morbidity, including bleeding, arrhythmia, or wound complications, except for 1 patient with a history of transient ischemic attack who developed a cerebrovascular accident (Table 1).

Follow-up

All patients were monitored and followed-up before discharge with an echocardiogram and within the first 6 months following surgery. The mean follow-up defined by the last available echocardiogram was 11.6 ± 10.4 months (median 8.1; interquartile range, 3.0-17.8) and was 100% complete. More than 25% of the cohort had greater than 17.8 months follow-up.

Assessment of AS, AR, and AS/AR by Echocardiography

Aortic regurgitation. Table 3 represents echocardiography data. When comparing preoperative with discharge echocardiogram in 51 patients with AR only and AR/AS, we found a reduction in mean indexed vena contracta/BSA jet width from preoperative (5.86 ± 2.17 mm/m^2) to discharge (1.35 ± 1.11 mm/m^2) (P < .001) and remained low at follow-up (1.71 ± 1.50 mm/m^2) (Figure 2, *A* and *B*). At discharge, 98% (56 of 57) of all patients had mild or less

TABLE 1. Operative/postoperative details

Variable	n or mean	% or SD
Patients	57	100%
Redo-sternotomy	40	70%
Partial sternotomy	5	9%
Leaflet material		
Autologous pericardium	20	35%
10 min	12	
2 min	8	
Photofix bovine pericardium	35	61%
CardioCel bovine pericardium	2	3.5%
Leaflet sizing		
Three equal leaflets	38	67%
Unequal leaflets	19	33%
Concomitant aortic valve procedure		
Sinus enlargement	20	35%
Aortic root enlargement	8	14%
Ascending aortic reduction	19	33%
Aortic root reduction	5	9%
Arch reconstruction	2	3.5%
Mitral valve repair/replacement	9	16%
Subaortic membrane	3	5%
Tricuspid valve repair	1	1.8%
Pulmonary valve repair/replacement	3	5%
Arch reconstruction	2	3.5%
Biventricular repair	1	1.8%
EFE resection	3	5%
Pacemaker	3	5%
ASD/VSD	4	7%
RV-PA conduit/PA plasty	6	11%
Mean cardiopulmonary bypass time (min)	156	57
Mean crossclamp time (min)	130	45
Required second cardiopulmonary bypass	6	11%
Anticoagulation strategy		
Aspirin only	31	54%
Aspirin and coumadin	25	44%
Lovenox only	1	1.8%
Median hospital length of stay, d [IQR]	6.4	[5.25-7.36]
Median Follow-up time, mo [IQR]	8.1	[2.96-17.76]

SD, Standard deviation; *EFE*, endocardial fibroelastosis; *ASD*, atrial septal defect; *VSD*, ventricular septal defect; *RV*, right ventricle; *PA*, pulmonary artery; *IQR*, interquartile range.

regurgitation. Freedom from moderate or greater AR (55 of 57 patients) was 97% at 1 year and 88% at 2 years. There were no factors identified that were associated with at least moderate AR at last follow-up, including age, BSA, weight, preoperative AR, preoperative disease (AS/AR), type of pericardium used, glutaraldehyde fixation time, or anticoagulation strategy.

Aortic stenosis. Intraoperative echocardiography revealed the mean aortic valve peak gradient for the 33 patients with AS and AS/AR preoperatively was 53.6 ± 22.2 mm Hg, decreased to 17.2 ± 9.6 mm Hg at discharge ($P < .001$), and remained stable at follow-up, 19.45 ± 18.3 ($P = .55$ compared with intraoperative) (Figure 3, *A* and *B*). Importantly, Figure 3, *B* shows that there was a decrease in the peak AS gradient in the early postoperative period, which was maintained. The 2 patients requiring reoperation had the greatest and most rapid rise in peak AS gradient, as shown in Figure 3, *B*. In total, 91% (42 of 46 patients with follow-up) of all patients had less than moderate AS at late follow-up. The 4 patients with at least moderate AS at last follow-up underwent the Ozaki procedure at a younger age, 7.3 ± 6.0 years versus 13.0 ± 5.6 years ($P = .06$) compared with the other 42 patients. No other factors were identified as predictive, as noted previously. Freedom from moderate or greater AS or AS/AR in all patients was 100% in the first year and 88% at 2 years.

Limited Mobility

Twelve patients (median age 6.2 years, range 2.2-15.5) were defined as having decreased leaflet mobility on follow-up echocardiography, with 5 patients having unequal leaflets. Right coronary leaflet had less mobility in 6 patients and noncoronary leaflet in 6. Seven patients had Photofix pericardium and 5 autologous pericardia (3 and 2 were treated with glutaraldehyde for 2 and 10 minutes, respectively). Six patients had aortic sinus (3) and root enlargements (3). Ten of these patients were on aspirin only and 2 were also on coumadin. We found an association between decreased leaflet mobility and anticoagulation therapy (exact $P = .047$; excludes 1 patient not on aspirin or coumadin): 16.7% of those with immobility were on aspirin and coumadin, compared with 52.3% of those with mobile leaflets. The risk of decreased leaflet mobility was increased 5-fold for those on aspirin alone compared with patients on aspirin and coumadin (odds ratio, 5.5, 95% confidence interval [CI], 1.1-27.9, $P = .04$) and more commonly occurred in patients developing more severe AS and AR ($P < .05$). Leaflet mobility was not associated with a preoperative indication of AR, AS, or AS/AR. After adjusting for preoperative aortic annulus z score, the estimated odds ratio for leaflet immobility in patients on aspirin alone versus those on aspirin and coumadin remained the same (odds ratio, 5.34; 95% CI, 1.04-27.49) and remained statistically significant ($P = .045$). When adjusted for type of leaflet material, the effect of aspirin alone is slight reduced (odds ratio, 4.16; 95% CI, 0.91-19.02, $P = .066$).

Assessment of LVEDV by Echocardiography

Among all patients, the mean z score of LVEDV (LVEDVz) significantly decreased from preoperative to discharge (3.65 ± 2.74 to 1.42 ± 2.53, $P < .001$) and remained low (1.42 ± 2.13, $P = .98$) over time. Factors associated with a lower LVEDVz at discharge included a greater preoperative grade of AS (slope ± SE –0.62 ± 0.19 per each increase in AS grade on a 6-grade scale, $P = .002$) and a

TABLE 2. Baseline characteristics

Characteristic	n or median	% or range
Patients	57	
Sex		
Male	21	37%
Female	36	63%
Age, y	12.43	[0.7-25.4]
<1	1	2%
1-5	7	12%
6-12	23	40%
13-17	17	30%
>18	9	16%
Weight, kg	44.3	[5.16-121]
0-10	1	2%
11-20	13	23%
21-40	13	23%
41-60	15	26%
>60	15	26%
BSA, m^2	1.33	[0.86-1.67]
Diagnosis		
Congenital aortic valve disease	29	51%
Truncus arteriosus	4	7%
Rheumatic/endocarditis disease	7	12%
Connective tissue disorder	4	7%
S/p arterial switch operation	5	9%
Other	8	14%
Prosthetic valve failure	5	
Bioprosthetic valve failure	4	7.02%
Mechanical valve failure	1	1.8%
Aortic valve morphology		
Unicuspid	9	16%
Bicuspid	20	35%
Tricuspid	26	46%
Quadricuspid	2	3.5%
Aortic valve pathology		
Aortic regurgitation	6	11%
Aortic stenosis	24	42%
Mixed	27	47%

BSA, Body surface area; *S/p*, status post.

lower preoperative grade of AR (P = .04). In addition, LVEDVz at discharge varied according to indication (P = .002), with an indication of AS only having the lowest mean z score (n = 4: –1.85), followed by mixed AS/AR (n = 26: 1.01), and AR only (n = 20: 2.61).

Assessment of Aortic Annulus, Aortic Root, and Ascending Aorta by Echocardiography

Preoperative echocardiography revealed the annulus long-axis view, annulus short-axis view, root, and ascending aortic diameters to be 20.9 ± 5.0, 25.1 ± 5.8, 25.8 ± 5.5, and 25.5 ± 7.4 mm, respectively. All patients demonstrated an increase in annular and root dimensions from discharge to late follow-up (P < .001), and there was no change in ascending aortic size (P = .15). The aortic annuli linearly increased from the date of surgery (time zero) to late follow-up (Figure 4). In the 8 patients who underwent annular enlargements, there was a mean increase from preoperative echo to discharge in annular z score of 0.83 ± 1.85 (P = .24) and an increase in annular size of 0.61 ± 2.61 mm (P = .53). The z score increased 0.96 ± 1.88 units from discharge to last follow-up (P = .22) and the size increased 2.4 ± 2.4 mm (P = .04). Figure 4 shows the trajectory of aortic annular growth over time, which is likely related to somatic growth. In patients with ascending aortic reduction, the ascending aorta was reduced from mean preoperative z score (n = 19) of 3.73 ± 2.76 to 1.14 ± 1.60 (n = 10) at last follow-up (median change –3.5, interquartile range –4.6 to 0.3, n = 9, P = .03) (Table 3).

Assessment of Leaflet Coaptation Height by Echocardiography

The mean leaflet coaptation height at discharge was 14.00 ± 3.45 mm and 12.24 ± 3.04 at late follow-up (P < .001).

Survival/Reoperation

Freedom from reoperation for aortic valve replacement was 91% at 1.5 years. Two patients developed significant mixed AS/AR requiring reoperation and aortic valve replacement at 7 and 3.75 months (Table 4). An additional patient undergoing an operation for biventricular repair underwent leaflet thinning at 11.4 months as a secondary procedure by resecting fibroelastic tissue on left leaflet. There were 2 deaths after discharge, one from a massive hemothorax in a patient requiring coumadin for a preoperative stroke and one whom had undergone reoperation and died due to multisystem organ failure.

DISCUSSION

AVRec has been applied to a wide spectrum of aortic valve disease in adult patients.[8-11] It allows natural aortic root expansion with maximal effective orifice preservation in systole.[12,13] The technique differs from other repair techniques whereby each of the 3 diseased individual leaflets are completely replaced with 3 autologous or bovine pericardial cusps.[14] Results in adults are promising; freedom from aortic valve reoperation was 96% and from recurrent moderate or greater AR was 93% at 4.5 years.[5] However, results in younger patients with congenital aortic valve disease remains unclear. We began AVRec in 2015 and report acceptable hemodynamics with no significant AR, low mean gradients, and annular growth in our first 57 consecutive congenital patients with aortic and truncal valve disease.

Following surgical aortic valvuloplasty for patients presenting with small preoperative aortic annuli and/or AS, persistent AS was common. In the series from Bacha and

TABLE 3. Differences in echocardiographic parameters throughout surgery and last follow-up

	All patients, mean ± SD (n)		AS indication, mean ± SD (n)		AR indication, mean ± SD (n)	
	Preoperative to discharge echocardiogram	Discharge to last F/U echocardiogram	Preoperative to discharge echocardiogram	Discharge to last F/U echocardiogram	Preoperative to discharge echocardiogram	Discharge to last F/U echocardiogram
VC/BSA, mm/m^2	–4.16 ± 2.21 (55)*	0.17 ± 1.36 (43)	–3.61 ± 2.04 (32)*	0.09 ± 1.24 (27)	–4.46 ± 2.01 (50)*	0.25 ± 1.41 (37)
Peak gradient, mm Hg	–23.73 ± 24.76 (48)*	1.38 ± 16.27 (43)	–36.74 ± 21.74 (30)*	1.32 ± 18.68 (26)	–19.97 ± 23.89 (42)*	2.78 ± 16.37 (37)
Mean gradient, mm Hg	–14.69 ± 15.59 (44)*	0.23 ± 7.64 (38)	–22.97 ± 14.13 (27)*	–0.25 ± 8.30 (23)	–11.90 ± 14.86 (38)*	0.96 ± 7.72 (32)
Coaptation height, mm	8.88 ± 4.85 (50)*	–1.76 ± 3.41 (37)	8.9 ± 3.82 (30)*	–1.87 ± 3.10 (23)*	8.91 ± 4.79 (45)*	–1.61 ± 3.51*
Annular diameter, mm	–1.81 ± 2.64 (56)*	1.72 ± 2.18 (43)*	–1.77 ± 2.78 (33)*	1.97 ± 2.38 (27)*	–1.81 ± 2.51 (50)*	1.69 ± 2.17*
Annular diameter/ BSA, mm/m^2	–1.13 ± 1.79 (56)*	0.65 ± 1.47 (42)*	–1.09 ± 1.81 (33)*	0.81 ± 1.51 (26)*	–1.16 ± 1.70 (50)*	0.56 ± 1.47 (36)†
Root diameter, mm	–1.41 ± 2.87 (55)*	2.16 ± 3.24 (43)	–1.02 ± 3.19 (33)†	2.32 ± 3.78 (27)*	–1.63 ± 2.82 (49)†	2.16 ± 3.07 (37)†
Asc Ao diameter, mm	–3.86 ± 6.06 (37)*	1.25 ± 4.14 (24)	–4.11 ± 6.84 (24)*	1.17 ± 5.13 (15)	–3.86 ± 6.28 (34)*	0.59 ± 3.76 (21)
LVEDV, mL	–41.67 ± 37.01 (47)*	8.34 ± 47.47 (30)	–44.06 ± 38.08 (29)*	16.27 ± 55.08 (19)	–43.02 ± 38.12 (43)*	5.23 ± 45.08
LVEDV z-score	–2.46 ± 2.21 (47)*	–0.01 ± 2.79 (29)	–2.37 ± 2.16 (29)*	0.68 ± 3.08 (18)	–2.54 ± 2.29 (43)*	–0.27 ± 2.45

SD, Standard deviation; *AS*, aortic stenosis; *AR*, aortic regurgitation; *F/U*, follow-up; *VC*, vena contracta; *BSA*, body surface area; *Asc Ao*, ascending aorta; *LVEDV*, left ventricular end-diastolic volume. *$P < .01$ vs zero change. †$P < .05$ vs zero change.

colleagues,[1] the single factor associated with moderate or greater postoperative AS was patients with moderate or greater preoperative AS. In the leaflet extension technique, excising only the cusp free edges leaves a thickened leaflet base and often leads to leaflet immobility and persistent gradients.[14] In this series, we showed no differences in outcomes when comparing patients based on their preoperative indication of AS, AR, or combined AS/AR. Also, in patients with AS, the mean aortic valve peak gradients decreased from 53 to 17 mm Hg, with 93% of patients having less than moderate AS at discharge. Furthermore, in patients with small annuli undergoing aortic root enlargements and AVRec, the native annuli continued to grow appropriately and remain free from AS.

Younger patients also have material factors to consider with AVRec, including pericardial degeneration, calcification, and growth potential. Optimal tissue and treatment regimen for leaflet reconstruction continues to be a major limitation for long-term success in AVRec. Due to limited success with other materials including cor-matrix, atrial tissue and pulmonary homograft, we continue to use autologous and bovine pericardium.[15,16]

Autologous pericardium has the theoretical potential of less antigenicity with or without glutaraldehyde treatment; however; glutaraldehyde predisposes to calcification.[17] Duran and colleagues[18,19] showed less fibro-calcific deterioration with autologous pericardium treated with 0.5% buffered glutaraldehyde for 10 minutes followed by rinsing in Ringer's lactate for 10 minutes compared with treated bovine pericardium at 8 years but no difference at 10 years. Importantly, these studies did not have anticalcification treatments applied and rinsing regimens were not always precisely managed leading to variability in residual glutaraldehyde and subsequent calcification. Therefore, AVRec protocol consists of three strict six-minute rinses in normal saline following 0.6% glutaraldehyde fixation.

There have been mixed results when using autologous pericardium for aortic valve repair. Liu and colleagues[20] published their long-term results of aortic valve replacement using autologous pericardium treated in 0.2% glutaraldehyde for 10 minutes in 15 young patients, with a mean age of 34 years and follow-up of 11.43 years, with a 33% reoperation rate. Jeong and colleagues[21] reported the long-term results of the leaflet extension technique using autologous pericardium, which was a similar treatment regimen (0.625% glutaraldehyde rinsed in three successive normal saline rinses) as reported by Ozaki. In that series, 41 patients with a mean age of 32 years had a 15% reoperation rate after 7 years, suggesting that an autologous pericardial patches may last longer than bioprosthetic aortic valves in young patients.[22] Myers and colleagues[23] reported in pediatric patients undergoing aortic valve repair where fresh autologous and Photofix-treated bovine pericardium trended toward better durability than glutaraldehyde-fixed bovine pericardium.

Photofix pericardium is prepared by a dye-mediated photooxidation method that avoids the use of glutaraldehyde, is biocompatible, resistant to calcification, and elicits

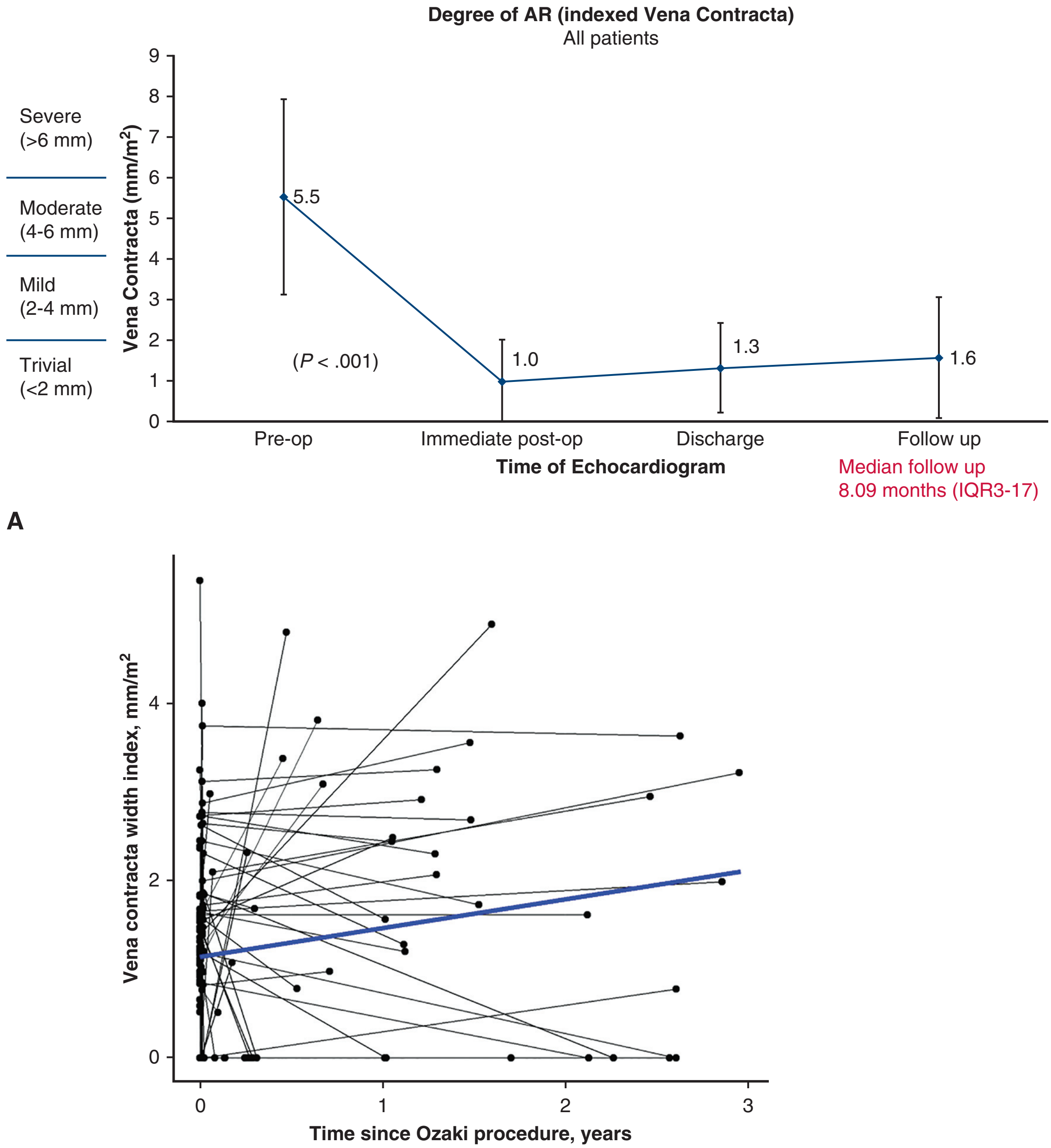

FIGURE 2. A, Vena contracta z score for body surface area represented as a mean ± standard deviation at preoperative, immediate post-intraoperative, discharge, and late follow-up time points. B, Trajectory of AR represented as vena contracta width index (mm/m^2) at the immediate post-intraoperative, discharge, and late follow-up time points. The *lines* represent individual patient trajectories and the *thick line* represents the weighted average of all patients' trajectories. Time zero represents the date of neoaortic valve reconstruction. Each patient is represented as a separate point/line. *AR*, Aortic regurgitation; *IQR*, interquartile range.

minimal inflammatory responses.[15,24,25] Baird and colleagues[24] reported on 490 implanted patches for congenital heart defects that demonstrated excellent performance and mild inflammation. Schoen and Levy[17] reported findings in 10 explanted CarboMedics Photofix-α valves between 8 and 23 months in which valve failure was characterized by multiple cuspal tears at valve commissures and/or basal attachment points near the Dacron cloth. There was marked hyalinization, loss of definition of collagen bundles and connective tissue cells, and no evidence of calcium, thrombus, or endocarditis.[17] In our aortic valve neocuspidization series, we used both autologous and Photofix bovine pericardium with similar rates of early failure but different mechanisms. Photofix showed excrescences with annular separation whereas autologous pericardium had calcified restricted leaflets that were concerning for endocarditis.

CardioCel is bovine pericardium that is subjected to an anticalcification tissue-engineering process that includes

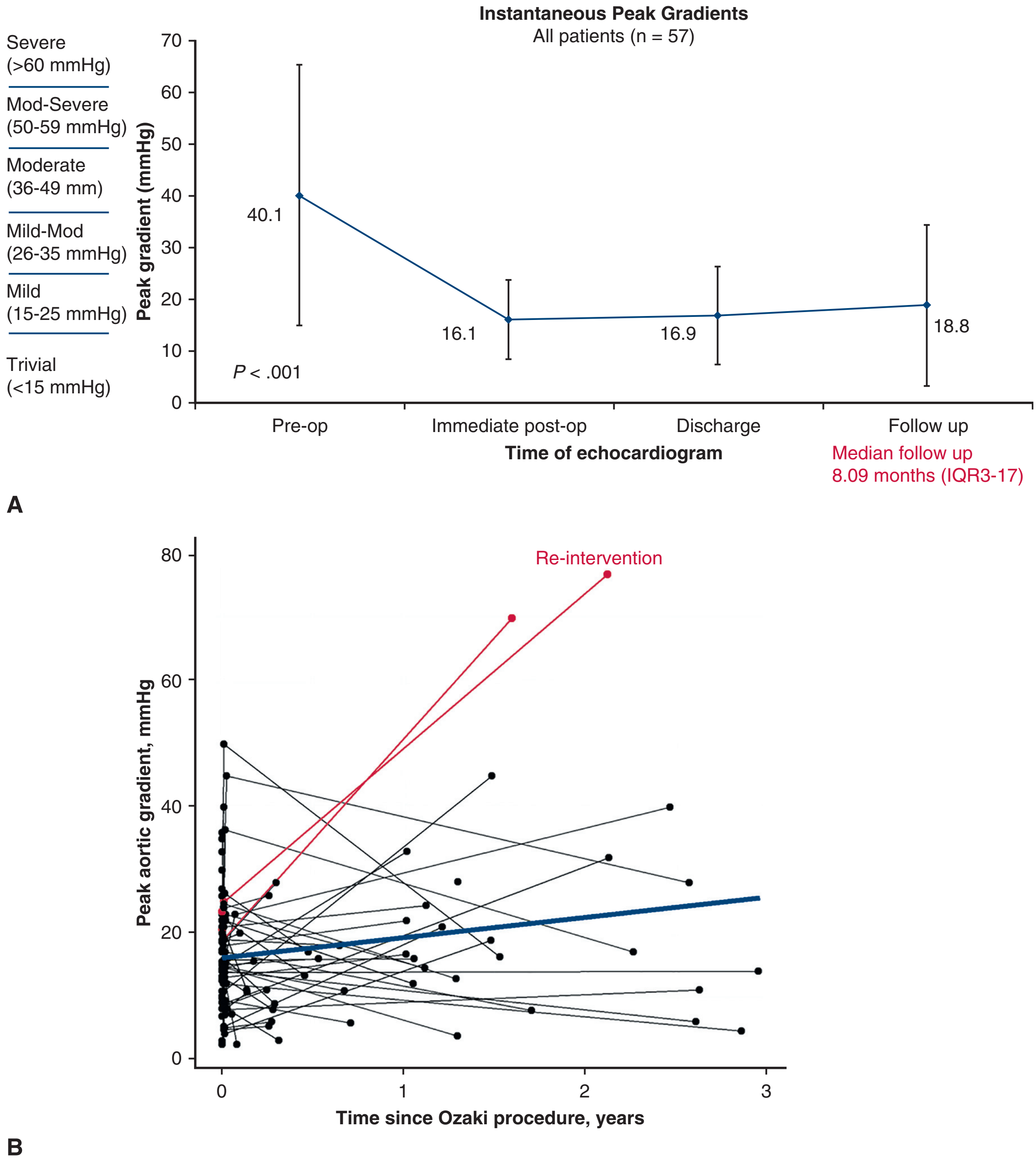

FIGURE 3. A, Preoperative, immediate post-intraoperative, discharge, and late follow-up mean peak pressure gradient through the aortic valve with echocardiography. Each *error bar* represents one standard deviation from the mean. B, Trajectory of aortic stenosis shows the peak aortic pressure gradient (mm Hg) at immediate post-intraoperative, discharge, and late follow-up time points. The *lines* represent individual patient trajectories and the *thick line* represents the weighted average of all patients' trajectories. Time zero represents the date of neo-aortic valve reconstruction. *IQR*, Interquartile range.

steps to reduce cytotoxicity by removing lipids, all cells and cell remnants, nucleic acids, and α-Gal epitopes followed by low-concentration glutaraldehyde crosslinking.[26] Mazzitelli and colleagues[27] reported on several patients using CardioCel with acceptable early results but limited late follow-up. Further follow-up is needed, as concerns remain for early calcification.

AVRec leaflet competence depends on material properties and direction, dimensions, and on how much the patch material deforms with diastolic pressure. Hofferberth and colleagues[28] reported on the deformability of fixed autologous, Photofix, and CardioCel pericardium over time. All materials exhibited nonlinear anisotropic mechanical response to equi-biaxial tension and with increasing

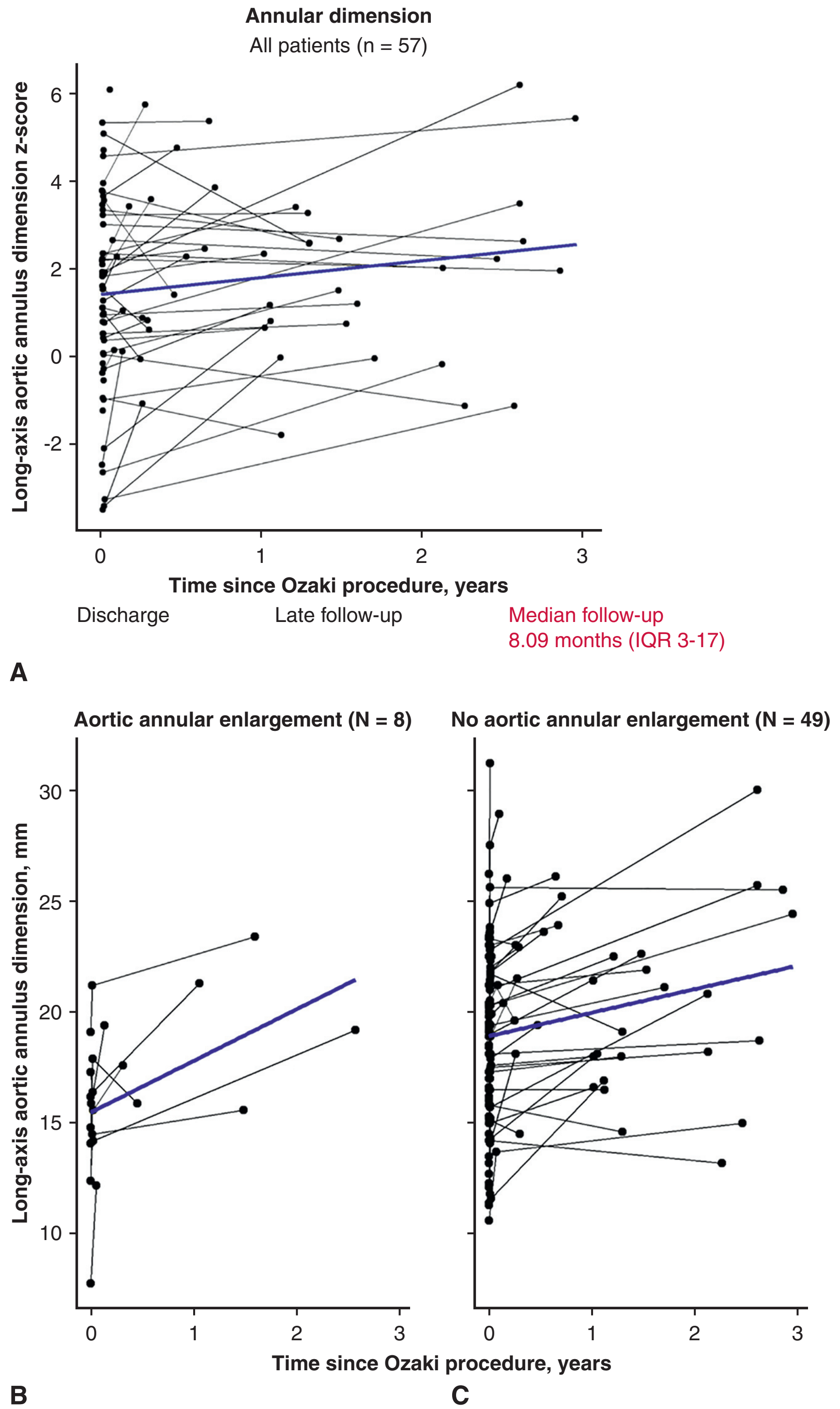

FIGURE 4. Trajectory of aortic annular growth over time. The *lines* represent individual patient trajectories based on the discharge and follow-up echocardiograms. Time 0 represents day of neo-aortic valve reconstruction. The *blue line* represents the weighted average of all patients' trajectories. The *panels* depict long-axis aortic dimension z score in A, all patients; B, patients undergoing annular enlargements, C, those with nonannular enlargements. *IQR*, Interquartile range.

glutaraldehyde fixation times, stretch uniformly decreased in both material directions. The Photofix response was similar to non–glutaraldehyde-treated pericardium. Since the AVRec leaflet sizers and templates were designed for autologous pericardium treated for 10 minutes, when shorter fixation times (2 minutes) or Photofix pericardium is used, leaflet shapes should be sized down to achieve optimal leaflet closure. In adult patients, Ozaki generally sizes up rather than down if between 2 sizes. Our experience suggests that sizing down may be more appropriate in

TABLE 4. Patients with greater than or equal to moderate AR or AS at latest follow up (n = 5)

	Moderate or greater AR*		Moderate or greater AS†		Moderate or greater AS *and* AR
Characteristic	Patient A	Patient B	Patient C	Patient D	Patient E
Primary surgery indication	AR	AR	AS/AR	AR	AS/AR
Age, y	2.2	2.3	14.2	7.8	10.5
Weight, kg	11	13.2	61.1	18	57.7
Native anatomy	Tricuspid	Tricuspid	Bicuspid	Tricuspid	Tricuspid
Preoperative history of endocarditis	No	No	No	No	No
Leaflet type	Photofix bovine	Autologous	Autologous	Autologous	Photofix bovine
Glutaraldehyde treatment, time, min	–	2	10	–	–
Leaflet sizing, mm (left, right, non)	15, 13, 15	17, 17, 17	19, 19, 21	21, 21, 21	25, 25, 25
Anti-coagulation	ASA	ASA	ASA	ASA + coumadin	ASA
Time to latest Echo, y	2.5	1.5	2.1	0.5	1.7
Reoperation	No	No	AVR	No	AVR
Indication for reoperation	–	–	AS	–	AS/AR
Time to reoperation	–	–	2.1 y	–	1.7 y
Pathology	–	–	Heavily calcified, uniformly thickened leaflets with fibrous overgrowth		Heavily calcified leaflet with pink/tan vegetations on both surfaces

AR, Aortic regurgitation; *AS*, aortic stenosis; *ASA*, aspirin; *AVR*, aortic valve replacement. *Measured by indexed vena contracta. †Measured by instantaneous peak gradient.

younger patients using Photofix and autologous pericardium fixed for 2 minutes.

The technical components of AVRec in pediatric patients are similar to those originally described for adults.[6] Cusps are sutured with a 3:1 ratio, and commissures are created with a deep stitch and an additional commissural suture. However, in addition to leaflet sizing, there are additional technical considerations that are important in younger patients. Most pediatric patients requiring aortic valve intervention have uni- or bicuspid valves. Ozaki reported using the raphe as a commissure to create a tricuspid valve; however, we have found that in younger patients this can give very asymmetric sinuses.[29] Thus, we often create 3 equal leaflets/sinuses based off the intracoronary commissure, which has provided several advantages. It places the coronary ostium in the middle of the sinus, making coronary obstruction unlikely, and allows for more uniform leaflet coaptation. The smaller the patient, the more critical the annular to sinotubular junction ratio becomes. We frequently augmented the noncoronary sinus to accommodate 3 equal leaflets creating similar annular and sinotubular junction dimensions. Intraoperative echocardiography is helpful in the assessment and revealing redundant and immobile leaflets when discrepancies exist.

In patients with bacterial endocarditis, long-term durability of aortic valve reconstruction using autologous pericardium compared with aortic valve replacement has been reported to show improved survival at 3 years but greater reoperation rates.[30] Ozaki and colleagues[10] demonstrated no adverse events after 34 months follow-up in 6 patients with endocarditis. Okada and colleagues[31] reported on a 21-year-old patient in whom there was no recurrence of infection after 4 years. In our series, we had 7 patients who had preoperative endocarditis, and none required reoperation. Continued follow-up is needed, but acceptable midterm results were obtained in patients undergoing AVRec reconstruction for endocarditis.

Several other reported advantages of AVRec are cost, need for only aspirin anticoagulation, and low embolic risk. Based on limited reports of patients having embolic complications following aortic valve reconstruction, initially we used aspirin only. However, it was recognized that subclinical leaflet thrombosis occurs frequently in transcatheter and bioprosthetic aortic valves, resulting in increased neurologic events. Makkar and colleagues[32] reported reduced leaflet motion on bioprosthetic aortic valves and the condition resolved with therapeutic anticoagulation. Anticoagulation with both aspirin and warfarin, but not dual antiplatelet therapy, was effective in prevention or treatment of subclinical leaflet thrombosis.[33] In our series, 83% of patients having decreased leaflet mobility were on aspirin only. Based on these findings, we began to use dual therapy with aspirin and warfarin for 3 months. Further investigation is warranted to determine an optimal anticoagulation regimen.

CONCLUSIONS

The AVRec or "Ozaki" procedure has excellent short-term results and should be considered for valve reconstruction in pediatric patients with congenital aortic and truncal valve disease. Longer-term follow-up is necessary to determine the optimal patch material and late valve function.

Conflict of Interest Statement

Drs Baird and del Nido have no financial relationships with JMODD or CryoLife but have had taught in sponsored courses by CryoLife. Dr Baird has also proctored cases associated with JMODD. All other 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.

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Key Words: Ozaki, AVNeo, aortic valve reconstruction, truncal valve reconstruction