Donor great vessel free arterial grafts for complex reconstruction during pediatric heart transplantation



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ABSTRACT

Objective: Prior studies suggest that prolonged donor heart warm ischemia time increases heart transplant mortality. Patients with single-ventricle heart disease requiring transplant with concomitant aortic arch or central pulmonary artery reconstruction present technical challenges that extend donor warm ischemia time using conventional techniques. Studies in larger pediatric and adult patients with single-ventricle anatomy have described the use of prosthetic material for concomitant great vessel reconstruction. We have used donor free arterial grafts to simplify concomitant great vessel reconstructions and reduce warm donor ischemia time in small patients with single-ventricle physiology undergoing heart transplant. The purpose of this study is to review our results in these patients.

Methods: Children with single-ventricle heart disease who underwent free donor arterial graft great vessel reconstruction at heart transplant were identified, divided into aortic arch and central pulmonary artery groups, and retrospectively reviewed. Warm and total ischemia times were recorded contemporaneously at transplant.

Results: Fifteen pediatric patients with single-ventricle physiology underwent donor free arterial graft great vessel reconstructions (9 aortic arch, 6 pulmonary artery). Mean donor warm and total ischemia times for the entire cohort were 52.8 \pm 10.7 and 341.7 \pm 41.2 minutes. Two patients required postoperative extracorporeal membrane oxygenation. Hospital survival was 94% (1 death). There were no late deaths, and 2 patients had late retransplant. There were no early or late aortic or pulmonary artery obstructions, reinterventions, or complications at median follow-up of 14.2 years (interquartile range, 4.2-16.3 years).

Conclusions: Donor free arterial grafts for concomitant great vessel reconstruction during heart transplant in small, single-ventricle patients reduces warm ischemia time, simplifies technical demands, and preserves growth potential. (JTCVS Techniques 2024;28:132-8)



Aortic reconstruction in patients with hypoplastic left heart syndrome during heart transplantation.

CENTRAL MESSAGE

Patients with single-ventricle heart disease pose significant challenges during heart transplantation, including the need for complex great vessel reconstruction.

PERSPECTIVE

This study highlights a strategy for heart transplant requiring concomitant great vessel reconstruction using donor free arterial grafts in pediatric patients with single-ventricle heart disease. This technique reduces technical demands, decreases donor heart warm ischemia time, and preserves growth potential.

See Discussion on page 139.

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As survival for patients with complex congenital heart disease improves, the population of patients with single-ventricle physiology presenting for heart transplant is expanding. ¹⁻³ This trend has increased the technical complexities commonly encountered in pediatric and congenital heart transplant programs. ^{3,4} Patients with coexisting aortic arch and or extensive pulmonary artery distortion, present at birth or as a result of prior

Abbreviations and Acronyms

AA = aortic arch

ECMO = extracorporeal membrane oxygenation

HLHS = hypoplastic left heart syndrome

PA = pulmonary artery PDA = patent ductus arteriosus

RV = right ventricle SVC = superior vena cava

interventions, are arguably the most challenging patients. Typically, great vessel reconstruction is accomplished using donor vessels procured and kept in continuity with the heart during implant. This method often presents technical challenges due to operative space limitations and high volume pulmonary venous return common in this population. Longer implant times (ie, donor warm ischemia) are necessary compared with simpler patients. One solution is to simplify transplant by reconstructing complex abnormal anatomy to near normal as a first intraoperative step before heart implantation. Iyengar and colleagues⁵⁻⁷ have promoted use of prosthetic conduits for great vessel reconstructions in a series of older children and adults with highly complex single-ventricle disease to limit donor ischemia time.

Prolonged allograft ischemia time is associated with worse outcomes. In a large pediatric registry report focused on heart allograft ischemia time, total ischemia time >4 hours was associated with increased early and late mortality.8 Total donor ischemia time is composed of cold and warm intervals. True warm ischemia time is not recorded in registries or most transplant programs. Two adult series examining the influence of estimated warm ischemia time demonstrated increased mortality with times >80 minutes. 9,10 In an analysis of our center's initial 50 infant heart transplants, we identified a trend toward higher hospital mortality when warm ischemia exceeded 70 minutes.¹¹ It is axiomatic that a given warm ischemia is more injurious than equivalent cold ischemia time. Based on this tenet, we developed a strategy that exchanges reduced warm ischemia time for a similar increase in cold ischemia time in complex patients undergoing concomitant great vessel intervention. Donor arterial free grafts are used for initial great vessel reconstruction while the donor cardiac mass remains in cold storage. Following reconstruction, the heart is implanted in a more standard fashion. This strategy relies on viable tissue with growth potential that is particularly advantageous in infants and smaller pediatric patients. The purpose of this study was to review our experience with this technique and to determine if great vessel complications occurred with patient growth.

METHODS

Patient Selection

All patients who underwent heart transplant at our free-standing pediatric center between January 2004 and March 2024 were reviewed. Patients with single-ventricle physiology were identified, and those who had concomitant aortic arch (AA) or extensive central pulmonary artery (PA) reconstructions were selected and grouped accordingly: AA group and PA group. Patients with biventricular disease, those in whom focal defects were repaired with small donor free tissue patches (eg, recurrent coarctation), and those who underwent atypical venous pathway reconstructions with donor free grafts were not assessed. Transplant hospitalization and follow-up data were obtained from patient medical records. This study was approved by our institutional review board and a waiver of individual consent requirement was granted (COMIRB #01-0506; November 1, 2023).

Surgical Technique

All transplants were performed at our institution. Our strategy was to restore implant anatomy to as near normal as possible and then proceed with heart implant. Great vessel reconstruction was planned and discussed with the organ recovery team to ensure recovery of adequate donor tissue. In general, vessels were procured in continuity with the heart: Aortic arch 1 to 2 cm beyond the ligamentum arteriosum, bilateral branch PAs beyond the upper lobar origins (when lungs were not recovered), and innominate vein in continuity with the superior vena cava (SVC). After recipient cardiectomy, reconstructive techniques were determined based on casespecific anatomic considerations. Donor free grafts were then removed keeping the myocardial mass submerged in cold solution. This is performed by harvesting donor great vessel tissue during organ recovery so that it may be retrieved for reconstruction keeping the allograft in cold storage. AA grafts were divided from the heart at the midascending aorta. PA grafts were divided from the heart at the mid-main PA 2 to 3 mm above the pulmonary valve. In 1 PA group, case donor lungs were recovered so the outer curve of the donor transverse AA was used as a free graft for central PA reconstruction. Intermittent circulatory arrest, and or antegrade cerebral perfusion were commonly used based on surgeon judgment. After great vessel reconstruction, the heart was removed from cold storage, and bicaval or biatrial (in infants) implantation was performed. Warm ischemia time, defined as the time from donor heart removal from cold storage to recipient aortic clamp release, was recorded contemporaneously. Total ischemia time was defined as the time between donor aortic clamping and recipient aortic clamp release.

Within each group, variations in reconstructive techniques were used depending on anatomic and donor tissue considerations. Two categories of arch reconstruction were used. Onlay patch of the beveled donor arch graft to the opened recipient arch similar to the original hypoplastic left heart syndrome (HLHS) transplant technique described by Bailey and colleagues. 12 If a coarctation shelf was present, reconstruction also included coarctectomy with posterior interdigitating distal arch advancement, ¹³ total arch replacement with end-to-end descending aortic anastomosis, and reimplantation of recipient arch branches. During heart implant the donor ascending aorta was anastomosed end-end to the donor free graft. For PA group patients, 3 reconstruction techniques (Tech 1 - PA reconstruction with donor PA as a patch; Tech 2 - PA reconstruction with donor aorta as a patch; Tech 3 - PA reconstruction using donor PA as an intact free graft) were employed after detachment of superior and inferior cavopulmonary connections. Recipient branch PAs were opened anteriorly as needed to relieve stenoses and connect the arteriotomy through cavopulmonary anastomotic defect(s) to create a single large defect. Reconstruction was completed with an onlay patch of posteriorly opened donor bilateral branch PAs kept in continuity with the main PA. In some cases, small superior cava detachment site defect(s) were patched with separate free patches of donor PA or aorta followed by a larger onlay free graft. If donor lungs were recovered, the convex outer curve of the donor transverse arch was used as a large onlay patch. The arch branches were closed with surgical clips, and the left-ward aspect of the patch was opened for end-side anastomosis of the donor main PA when the heart was implanted. Bilateral hilar end-to-end branch PA anastomoses were created using the intact free donor graft PA bifurcation in continuity with the main PA. In all cases, grafts were tailored to position the donor main PA stump for conventional end-to-end anastomosis.

Follow-up

Echocardiograms and cross-sectional imaging (when available) were reviewed to assess reconstructed great vessel pathway patency. Surveillance catheterizations were reviewed to assess for left ventricle to femoral artery gradients in the AA group and right ventricle (RV) to branch PA gradients in the PA group. Follow-up data were collected from the most recent clinic note. Patient somatic growth was quantified by determining a "growth multiple" (most recent follow-up weight/weight at transplant).

Statistical Analysis

Reconstruction type, warm and total ischemia times, complications, follow-up noninvasive imaging, hemodynamic data, and survival were analyzed. Patients who underwent retransplant were censored at second transplant. Statistical analyses were conducted using Stata version 14 (Stata Corp). Descriptive statistics for continuous variables were listed as mean \pm SD for parametric data or median (interquartile range [IQR]) for nonparametric data. Categorical data were listed as n (%).

RESULTS

In total, 307 patients were transplanted during the study interval. Fifteen patients (9 AA group, 6 PA group) met inclusion criteria and were reviewed. Baseline data are summarized in Table 1. All AA group patients were infants with HLHS. All PA group patients were small (median age, 4.99 years; maximum weight, 33 kg). Mean donor to recipient weight ratios were > 2:1 in both groups. Mean total and warm ischemia times for the entire cohort were 342 \pm 41 and 53 \pm 11 minutes, respectively. Median follow-up was 14.2 years (IQR, 4.2-16.3 years). The mean growth multiple for the entire cohort was 7.0 \pm 5.4.

Hospital survival was 94%. Two patients required posttransplant venoarterial extracorporeal membrane oxygenation (ECMO). Hospital mortality occurred in 1 AA group patient with HLHS and obstructed supracardiac pulmonary venous return of the right lung. This patient underwent multiple ascending pulmonary vein stents, ductus arteriosus stent, and open bilateral PA bands in advance of heart transplant. Persistent pulmonary hypertension and profound right lung complications led to secondary RV function and death despite venoarterial ECMO. One AA patient had severe primary graft dysfunction that required venoarterial ECMO (7 days). This patient had HLHS with Ebstein anomaly and severe tricuspid regurgitation. Due to deteriorating clinical condition, a marginal donor was accepted. The patient survived to discharge, but was re-transplanted at 1 year for persistent diastolic heart failure and remains alive. One other AA group patient was retransplanted at 15.9 years for graft coronary artery vasculopathy. Given the young age and length of follow-up for the entire cohort, growth was substantial (mean growth multiple of 7.0 \pm 5.4). No patients

TABLE 1. Baseline data by great vessel reconstruction

Category	Aortic arch	Pulmonary artery reconstruction
Total	9	6
Underlying diagnosis Hypoplastic left heart	100 (9)	50 (3)
syndrome Tricuspid atresia	_	16.7 (1)
Pulmonary atresia/intact ventricular septum	-	16.7 (1)
Double outlet right ventricle, mitral atresia	_	16.7 (1)
Age at transplant (y)	0.19 (0.05-0.43)	4.99 (1.35-10.1)
Weight at transplant (kg)	4.7 ± 1.7	16.7 ± 10.2
Donor to recipient weight ratio	2.2 ± 0.8	2.2 ± 0.6
Ischemia time (min) Warm ischemia time Total ischemia time	47 ± 5 341 ± 48.7	62 ± 11 342 ± 31
Use of extracorporeal membrane oxygenation	22 (2)	0
Hospital survival	88.9 (8)	100 (6)
Follow-up time (y)	8.4 (6.6-14.9)	14.4 (6.0-15.2)
Follow-up growth multiple	9.2 ± 4.3	4.2 ± 2.9

Values are presented n, % (n), mean \pm SD, or median (interquartile range).

demonstrated evidence of great vessel obstruction on follow-up echocardiogram, routine hemodynamic assessment, or cross-sectional imaging, and no patient has undergone posttransplant great vessel reintervention.

AA Reconstruction Group

Table 2 summarizes the AA group. All patients had HLHS with a primary heart transplant treatment strategy. Complicating anatomic factors were present in 5 patients (2 anomalous pulmonary venous return, 1 RV-dependent coronary circulation, 1 Turner syndrome with intact atrial septum, and 1 Ebstein anomaly). Four patients had primary transplant per parent preference. Four patients had no prior intervention: 2 patent ductus arteriosus (PDA) stent only, 1 ascending pulmonary vein confluence stent with PDA stent and open bilateral PA bands, 1 atrial septostomy stent with PDA stent and open bilateral PA bands, and 1 PDA stent with open bilateral PA bands. Onlay free AA patch was used in 7 patients (4 with coarctectomy and interdigitating posterior arch advancement). Two patients had total arch replacement: 1 with a recipient arch branch Carrell patch, and 1 with recipient arch branch revascularization by anastomosis of the donor innominate artery to the opened recipient distal ascending-proximal transverse arch (Figure 1). Significant additional reconstructions were required in 3 AA group patients: 2 repairs of anomalous pulmonary venous return

TABLE 2. Aortic reconstruction patient cohort

Aortic reconstruction group							
Patient	Underlying diagnosis	Reconstruction	Warm ischemic time (min)	Total ischemic time (min)	Follow-up (y)	Survival at latest follow-up	Aortic arch repair gradient at 1 y
11-mo-old boy	HLHS, dextrocardia, DORV, RV dependent coronaries, after PA bands	Total AA replacement, recipient arch anastomosed to donor innominate artery, RPA band site patch with donor PA	49	351	0.68	Yes	N/A
3-mo-old boy	HLHS, TAPVR, after PDA stent	Onlay AA patch; coarctectomy; TAPVR repair	46	440	4.2	Yes	0
2-wk-old boy	HLHS	Onlay AA patch	50	353	8.4	Yes	0
7-mo-old boy	HLHS, IAS, Turner syndrome, PA bands, atrial septal stent, PDA stent	Onlay AA patch	50	375	14.9	Yes	0
2-wk-old boy	HLHS, bilateral SVC	Onlay AA patch, coarctectomy	44	279	16.5	Yes, re-HTx at 15.9 y	2
2-mo-old girl	HLHS, PDA stent, PA bands	Onlay AA patch	53	303	17.5	Yes	0
6-mo-old boy	HLHS, PAPVR, ascending PV stent, PDA stent, PA bands	Onlay AA patch, coarctectomy, PAPVR repair	38	339	7 d	No	N/A
6-wk-old boy	HLHS, Ebstein, severe TR	Onlay AA patch, coarctectomy	49	340	6.7	Yes, re-HTx at 1 y	6
17-d-old girl	HLHS	Total arch replacement with Carrel patch	43	291	16.4	Yes	5

HLHS, Hypoplastic left heart syndrome; DORV, double outlet right ventricle; RV, right ventricular; PA, pulmonary artery; AA, aortic arch; RPA, right pulmonary artery; N/A, not available; TAPVR, total anomalous pulmonary venous return; PDA, patent ductus arteriosus; IAS, intact atrial septum; SVC, superior vena cava; re-HTx, redo heart transplant; PAPVR, partial anomalous pulmonary venous return; TR, tricuspid regurgitation.

and 1 right branch PA band site patch with donor free PA graft. Mean AA group total and warm ischemia times were 341 \pm 49 minutes and 47 \pm 5 minutes. Overall patient and graft survival at median follow-up of 8.4 years (IQR, 6.6-14.9 years) was 89% (n = 8; 1 early death) and 67% (n = 6; 1 early death and 2 retransplants), respectively. All hospital survivors had normal echocardiographic flow in the ascending and descending aorta. Left heart hemodynamics in the 7 patients who reached the 1-year surveillance catheterization demonstrated a mean systolic left ventricle to femoral artery gradient of 1.9 \pm 2.7 mm Hg.

PA Reconstruction Group

Table 3 summarizes the PA group. All 6 patients had prior single ventricle palliation: 3 completion Fontan and 3 stage-2 bidirectional Glenn. Four underwent reconstruction by onlay donor free PA grafts with opened branch PAs in continuity with the main PA (Figure 2). One had hilum-to-hilum onlay patch with a donor free transverse arch graft and donor main PA anastomosis to an opening in the patch and 1 had bilateral hilar level end-end branch PA anastomoses using a donor free PA graft with the intact bifurcation in

continuity with the donor main PA. Additional reconstruction was necessary in 1 patient who had an onlay PA graft reconstruction to connect a left SVC to the donor SVC using a free graft conduit fashioned from the donor transverse AA. At long-term follow-up, this SVC reconstruction remains patent and has had no evidence of obstruction or gradient across the reconstruction.

Mean total and warm ischemia times were 343 ± 31 and 62 ± 11 minutes, respectively. Hospital, late, and graft survivals were 100% at a median follow-up of 14.4 years (IQR, 6.0-15.2 years). No PA group patient had primary graft dysfunction. All echocardiograms demonstrated normal main and branch PA flow. There were no pulmonary artery reinterventions. Late right heart hemodynamics demonstrated no significant systolic RV to branch PA gradients (range, 0-6 mm Hg).

DISCUSSION

The number of patients with single-ventricle physiology presenting for transplant is increasing. Dense adhesions and fused pleural spaces often limit exposure. Plethoric collateral pulmonary return that is the norm hinders exposure

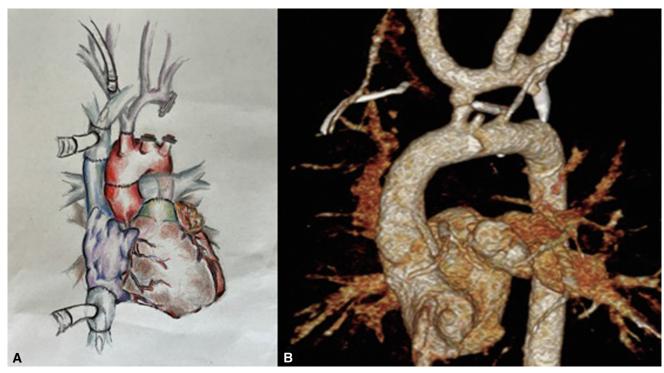


FIGURE 1. Aortic Arch Reconstruction illustration (A) and postoperative 3-dimensional CT scan imaging (B). This recipient underwent total arch reconstruction via arch branch revascularization by anastomosis of the donor innominate artery to the opened recipient distal ascending-proximal transverse arch.

and promotes graft rewarming during implant. Large donor to recipient size mismatch, common in infants and smaller patients, further crowds exposure. Up to 10% of failing Fontan patients require concomitant AA reconstruction, and more than 50% require extensive central PA reconstruction. For these reasons, patients requiring concomitant great vessel reconstruction arguably constitute the most challenging transplant cases. With typical implant methods, donor vessels are kept in continuity with the heart and used for AA or central branch PA reconstruction. 12,14,15 Long suture lines and technical challenges due to these factors significantly increase total and warm ischemia time. Strategies to address these challenges are increasingly important.

Because prolonged donor warm ischemia is an important risk factor for primary graft dysfunction and death, ⁹⁻¹¹ we developed the strategy detailed in this study. Our approach shifts the most complex part of the transplant to the interval of donor cold ischemia. This reduces the workload required during warm ischemia in exchange for longer cold ischemia. Because there is no interference from the donor cardiac mass, exposure is excellent and surgical efficiency is improved. The incidence of primary transplantation for HLHS has decreased and is now reserved for patients at excess risk for staged palliation. We included the AA group in this study because separating the arch reconstruction from the heart implant

offers the same advantages accrued with free donor grafts in failing Fontan patients undergoing PA reconstruction. This study is the first in which donor warm ischemia time was measured rather than estimated. Considering the complexity, the warm ischemia times in the AA group (47 \pm 5 minutes) and PA group (62 \pm 11 minutes) were very reasonable. Only 1 case had primary graft dysfunction. The warm ischemia time was only 49 minutes, and poor donor quality was the likely cause.

We are not the first group to report the strategy of initial intraoperative conversion of complex recipient anatomy to more normal anatomy to simplify heart transplantation with concomitant great vessel reconstruction. Iyengar and colleagues⁵ reported a similar approach in which prosthetic conduits were used for extensive AA and PA reconstructions. Their median age at transplant was 15 versus 5 years in our comparable PA group. Use of prosthetic material permits reconstruction before donor heart arrival thereby significantly reducing total and warm ischemia time. In a minority of cases they used free donor vessel grafts, presumably in small patients. Brink and colleagues¹⁶ also described a case in an adult using a free donor aortic conduit for central PA replacement. We have also used nonviable material for advance reconstructions in larger patients that were not included in this series. The oldest patient in the current study was aged 18 years and weighed 33 kg. This

TABLE 3. Pulmonary artery reconstruction patient cohort

Pulmonary artery reconstruction								
			Warm ischemic	Total ischemic	Follow-up	Survival at latest	PA gradient at	
Patient	Underlying diagnosis	Reconstruction	time (min)	time (min)	(y)	follow-up	latest cath	
6-y-old girl	HLHS, after Fontan with heart failure and PLE	Donor bilateral PA free graft technique: Donor free PA graft used for bilateral hilar level end-end branch PA anastomoses with contiguous MPA before donor heart implantation	79	366	14.4	Yes	6	
18-y-old girl	Tricuspid atresia, VSD, DORV status post-Fontan palliation	Donor bilateral PA free graft technique: Recipient hilum-to-hilum PA reconstruction with only donor PA free graft. Left SVC reconstruction using donor aortic arch free graft	49	305	5.5	Yes	0	
1-y-old boy	PA/IVS, Pulmonary vein stenosis s/p bidirectional Glenn	PA patch reconstruction technique: Corrected distal RPA stenosis using onlay patch of opened RPA in continuity with MPA	61	358	14.9	Yes	6	
1-y-old boy	HLHS after Glenn, with severe AV valve insufficiency	PA patch reconstruction technique: Hilum to Hilum and MPA reconstruction using donor aorta as patch	53	371	19.4	Yes	4	
4-y-old boy	HLHS after Glenn, severe left PA hypoplasia	PA patch reconstruction technique: RPA patched to middle lobar level with free PA patch and anastomosed MPA to leftward side of onlay patch out into the LPA	57	353	2.4	Yes	4	
10-y-old boy	Single Ventricle s/p PA band, Glenn, Fontan with heart failure and PLE	Donor bilateral PA free graft technique: RPA to LPA donor free graft Onlay patch with contiguous MPA	71	302	13.5	Yes	1	

PA, Pulmonary artery; HLHS, hypoplastic left heart syndrome; PLE, protein losing enteropathy; MPA, main pulmonary artery; VSD, ventricular septal defect; DORV, double outlet right ventricle; SVC, superior vena cava; IVS, intact ventricular septum; RPA, right pulmonary artery; AV, atrioventricular.

patient has subsequently grown to 43 kg. In our view reconstruction with nonviable material should be reserved for patients in whom growth potential is not a consideration.

Donor hearts implanted in infants and children adapt to the recipient circulation and grow appropriately with the patient. The Great vessel growth in pediatric recipients has not been assessed. However, it clearly occurs based on our extensive clinical experience with retransplanted patients first transplanted in infancy. The growth multiples observed in our patients demonstrate significant growth in both groups during follow-up. The absence of any significant

great vessel pathway obstructions with serial noninvasive and invasive assessments over lengthy follow-up time indicates that great vessel reconstructions grew or at least enlarged appropriately.

This study has several limitations, including the retrospective nature and small sample size. There is no other cohort of patients in whom the technical challenges are comparable; thus, we have no control group to better define our conclusions. Lastly, in the absence of histologic data, we cannot definitely state that the enlargement of reconstructed great vessels observed in these patients resulted from true tissue growth.



FIGURE 2. Pulmonary artery reconstruction illustration. The *blue portion* indicates the donor hilar to hilar free graft used for reconstruction to recipient bilateral distal branched pulmonary arteries with anastomoses performed at the hilar level bilaterally.

CONCLUSIONS

As the population of single-ventricle patients presenting for transplantation continues to grow, strategies to address the challenges of reconstruction and mitigate the risk of prolonged ischemia will become increasingly important. This study highlights a useful strategy for concomitant great vessel reconstructions during heart transplant that affords growth potential and reduces donor warm ischemia with excellent long-term results.

Webcast (

You can watch a Webcast of this AATS meeting presentation by going to: https://www.aats.org/resources/complex-great-vessel-reconstru-7218.



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.

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Key Words: single ventricle, congenital heart disease, pediatric heart transplantation