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Valve Replacement in Children with Single Ventricle Physiology

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Abstract

Severe atrioventricular valve (AVV) or semilunar valve (SLV) regurgitation in the setting of a single ventricle physiology may proceed to valve replacement if repair strategies fail. Outcome data for these children are limited. We present transplant-free survival of a case series of children with single ventricle physiology undergoing either atrioventricular replacement (AVVR) or semilunar valve replacement (SLVR) from a multi-institutional, US-based registry (Pediatric Cardiac Care Consortium—PCCC). Outcomes were derived from PCCC and by linkage with the National Death Index (NDI) and Organ Procurement Transplant Network (OPTN). Fifty children with single ventricle physiology were identified to have received either AVVR ($n = 38$) or SLVR ($n = 12$). There were 17 in-hospital deaths including 8 intraoperative deaths (all intraoperative deaths were among children requiring AVVR). The in-hospital mortality was 42% and 8% for AVVR and SLVR, respectively. Among the 33 children surviving to hospital discharge, follow-up was available in 15 (46%). Death or cardiac transplant after hospital discharge occurred in 10—death in 4 (all among those requiring AVVR), cardiac transplant in 6 (2 following AVVR, 4 following SLVR). Valve replacement in children with single ventricle physiology, especially AVVR, is associated with poor outcomes. Alternative palliation strategies should be considered in children with single ventricle physiology with significant AVV or SLV regurgitations.

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Keywords

Atrioventricular valve replacement; Semilunar valve replacement; Single ventricle physiology; Single ventricle palliation

Background

Atrioventricular valve (AVV) regurgitation that is hemodynamically significant occurs in over a third of children with single ventricle physiology [1, 2]. In a single center report, prevalence of semilunar valve (SLV) regurgitation in children with hypoplastic left heart syndrome was up to 61% overtime [3]. This high prevalence of AVV or SLV regurgitation in a single ventricle physiology circulation may be due to a volume-overloaded state leading to progressive ventricular/annular dilatation or due to inherent structural abnormalities of the valve. Preservation of the native valve via repair remains the ideal choice of management of valve failure [1, 4–8]. However, valve dysfunction can be severe, repair techniques may fail, or repair efforts are futile, requiring valve replacement in some children [1, 2, 8].

Several large studies with long-term follow-up have reported outcomes of prosthetic valve replacement in children with two-ventricle physiology congenital heart disease [9, 10]. However, data regarding outcomes following valve replacement in children with single ventricle physiology are limited [2, 8]. The objective of this study is to describe long-term, transplant-free survival of children with single ventricle physiology undergoing either atrioventricular valve replacement (AVVR) or semilunar valve replacement (SLVR), using a multi-institutional database (Pediatric Cardiac Care Consortium—PCCC) linked with the National Death Index (NDI) and the Organ Procurement Transplant Network (OPTN) registries.

Methods

This is a retrospective study using data from the PCCC, a US-based database of cardiac surgical and transcatheter interventions performed in 44 participating centers between 1982 and 2003 on over 137,000 patients [11–13]. We queried the registry for either AVVR or SLVR procedures in children aged younger than 21 years at intervention, with underlying single ventricle physiology, entering the database between the registry's initiation (January 1, 1982) and April 15, 2003 (date of stricter implementation of Health Insurance Portability and Accountability Act, precluding further linkage analyses). During this period, PCCC had enrolled 3807 patients with single ventricle physiology [14]. Of these, 50 patients who underwent AVVR or SLVR and had the necessary clinical records were identified.

The PCCC includes information on all cardiac procedures performed, cardiac diagnoses, presence of genetic/chromosomal abnormalities and other major non-cardiac conditions, and in-hospital deaths. Additional data were abstracted from the clinical reports submitted to PCCC including the type of SV valve replacement (AVVR versus SLVR), systemic LV versus systemic RV, age and body weight at AVVR or SLVR surgery, race/ethnicity (when available), prosthetic valve size and type, previous cardiac surgeries including attempts at AVV or SLV repair, and discharge status. (See Supplemental Table 1).

Identifiers used for linkage with NDI and OPTN included first and last name, date of birth, sex, and state of last known residence. Data provided by NDI included date and cause of death, and OPTN provided information on listing and receipt of cardiac transplant including date transplanted. Linkage data from the NDI and OPTN¹ registries of children meeting inclusion criteria were obtained to determine long-term, survival, and cardiac transplant status through December 2014. The methodology and sensitivity of linkages to NDI and OPTN have been reported and reach 89 and 90% for the NDI and OPTN, respectively [13, 15].

Results

Among 3,807 patients < 21 years of age with single ventricle physiology, 50 (1.3%) met inclusion criteria (Fig. 1). Of them, there were 38 who underwent AVVR (all mechanical) and 12 underwent SLVR (4 bio-prosthetic, 8 mechanical). Baseline demographics and other characteristics are presented in Table 1. The two leading primary cardiac diagnoses were tricuspid atresia in 14 (28%) and double inlet left ventricle in 11 (22%). Valve repair was attempted in 9 children [8 AVVR, 1 SLVR]: six prior to valve replacement surgery and three at the time of valve replacement surgery. All cases requiring valve replacement had a background of regurgitation. Mechanical prosthesis was used in 47 (94%) with all 38 AVVR being mechanical and 8 of the 12 SLVR being mechanical. Twenty-eight (56%) of valve replacement occurred at or post-Fontan which comprises 1.9% of the subgroup ($n = 1508$) reaching Fontan stage in PCCC (Table 2). Only 7 of the 23 children who had valve replacement pre-Fontan proceeded to the completion of Fontan.

There were 8 intraoperative deaths (all in children requiring AVVR) with an additional 9 deaths occurring prior to hospital discharge for a total of 17 in-hospital deaths [16 AVVR, 1 SLVR]. The in-hospital mortality was 42% and 8% following AVVR and SLVR, respectively. No cardiac transplants were performed in either group prior to hospital discharge. The disposition of all children and those surviving to hospital discharge is detailed in Fig. 2a, b. Death or cardiac transplant after hospital discharge occurred in 10; death in 4 children, all associated with AVVR and cardiac transplant in 6, 2 following AVVR, 4 following SLVR. We compared characteristics of those who had follow-up/identifiers for linkage to those who had no follow-up as they lacked identifiers for linkage. Those who could not be linked were older and heavier at time of AVVR or SLVR. (See Supplemental Table 2).

Of those surviving to hospital discharge, average time to death or cardiac transplant following AVVR or SLVR was 2.4 years (IQR 1.1–3.9) and 4.7 years (IQR 1.4–8.2), respectively. For those alive without transplant at the end of the study period ($n = 5$), median follow-up was 15.4 years (IQR 14.6–16.2) (Fig. 3). (Key variables of each child presented in Supplemental Table 3).

¹This study used data from the OPTN. The OPTN data system includes data on all donor, wait-listed candidates, and transplant recipients in the USA, submitted by the members of the OPTN. The Health Resources and Services Administration, U.S. Department of Health and Human Services provides oversight to the activities of the OPTN contractor.

Discussion

We used a multicenter US-based clinical registry with linkage to national event tracking registries to describe the rarely reported outcomes of children with single ventricle physiology undergoing valve replacement. AVVR or SLVR is a rare resort procedure for children with single ventricle physiology and, in our cohort, accounted for a very small percentage (< 2%) of the palliated single ventricle physiology patients and the subgroup reaching Fontan stage. Because of this rarity, very little information becomes available on their long-term outcomes from single centers, thus requiring multicenter or registry-based observations.

Our data indicate poor prognosis in those who underwent valve replacement, particularly when the atrioventricular valve is involved. In-hospital mortality for AVVR was high in our case series. Our cohort also conveyed that significant attrition rate due to death or cardiac transplant persists among children discharged alive from the hospital. King et al. reported that atrioventricular valve failure is frequent in those with single ventricle physiology and associated with a higher prevalence of Fontan failure. In their cohort of single ventricle physiology cases from across Australia and New Zealand, 8 of 13 children who underwent AVVR died or were transplanted; these poor outcomes are similar to our observation [2]. A recent Japanese, multicenter report noted that 20 of 56 children (36%) with palliated single ventricle physiology who underwent AVVR had died during the 3.7 ± 2.6 -year follow-up [8]. Our data and the observations from these two studies convey the uniformly poor outcomes following AVVR in single ventricle palliated children across the world. While in-hospital mortality for SLVR in our small case series was not as high as following AVVR, their long-term outcomes are even less understood.

AVV or SLV competency is an important factor that determines long-term survival and quality of life in those with single ventricle physiology. Some suggest that it is best if AVVR is performed before the Fontan procedure in order to improve the pre-Fontan hemodynamics, as the Glenn stage is more forgiving than the Fontan physiology [2, 16]. PCCC data for transplant-free survival for all children with palliated single ventricle physiology were 89% at 15 years postoperatively [15]; however, survival was less than 50% at 15 years postoperatively in those who underwent AVVR and SLVR.

Overall, valve failure proceeding to replacement in single ventricle physiology in our cohort, especially AVVR, was a risk factor for premature mortality. Timing of valve replacement or other palliative strategies such as cardiac transplant needs further investigation for these challenging children.

Limitations

Data collection was limited to variables collected by the PCCC and by the incomplete nature of long-term follow-up by NDI/OPTN linkage methodology. OPTN linkage did not span the entire period of this data collection. Also, the PCCC database represents operations performed during a prior era, more than 15 years ago and therefore, current outcomes may be different. Based on age and weight distribution of those who could not be linked, it is

possible that their outcomes maybe have been better. Thus, these outcomes data are a conservative estimate. Details of the mechanisms and severity of valve failure could not be ascertained. In addition, re-interventions including re-do valve replacements or additional procedures such as need for pacemaker implantation could not be tracked, precluding analysis of these morbidities. Despite these limitations, we believe that this report adds information regarding the outcomes of a large US cohort in terms of children-years of follow-up for the rare occurrence of AVVR or SLVR in the context of single ventricle physiology circulation.

Conclusion

Valve replacement in single ventricle physiology, especially AVVR, is associated with poor outcomes. Optimal timing for valve replacement or timing for referral for cardiac transplant in such children needs further investigation.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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**Atrioventricular valve replacement*

***Semilunar Valve replacement*

Fig. 1.
Inclusion and exclusion criteria

**Atrioventricular valve replacement*

**Semilunar valve replacement*

Fig. 2.

a Outcomes of children with single ventricle palliation following AVVR. **b** Outcomes of children with single ventricle palliation following SLVR. AVVR atrioventricular valve replacement, SLVR semilunar valve replacement

**Atrioventricular valve replacement*

***Semilunar Valve replacement*

Fig. 3.
Survival following AVVR and SLVR (includes in-hospital deaths). *AVVR* atrioventricular valve replacement, *SLVR* semilunar Valve replacement

Table 1

Demographics of single ventricle palliated children following AVVR or SLVR

	AVVR N = 38	SLVR N = 12
Age at surgery (years) (IQR)	8.7 (3.5–14.5)	4.3 (0.1–11.1)
Weight at surgery (Kg) (IQR)	22.0 (12.5–39.5)	15.4 (3.96–33)
Male N (%)	23 (61)	8 (67)
Mechanical valve N (%)	38 (100)	8 (67)
Valve replacement Post-Fontan N (%)	14 (37)	8 (67)
Systemic LV N (%)	30 (79)	6 (50)

P values between variables for AVVR and SLVR were not significant *AVVR* Atrioventricular valve replacement, *SLVR* Semilunar valve replacement

Table 2

Timing of valve replacement in relation to single ventricle palliation stages

	Total <i>N</i> = 50	AVVR <i>N</i> = 38	SLVR <i>N</i> = 12
With stage 1	1	1	0
Pre-Glenn	8	6	2
With Glenn	4	2	2
Pre-Fontan	9	9	0
With Fontan	6	6	0
Post-Fontan	22	14	8

AVVR Atrioventricular valve replacement, *SLVR* Semilunar valve replacement