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Original Article

Perioperative Outcomes in Patients With Failing Single-Ventricle Physiology Undergoing Ventricular Assist Device Placement: A Single Institutional Experience

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Objective: To address the current lack of specified data existing regarding the perioperative characteristics and outcomes in a novel patient population, which may bridge the current understanding of how patient characteristics and perioperative management may influence the postoperative hospital course before cardiac transplantation.

Design: A retrospective electronic chart review included all patients with failing single- ventricle (SV) physiology receiving ventricular assist device (VAD) support at a high-volume pediatric VAD center between April 5, 2010, and December 1, 2020, using institution-based electronic medical records for retrospective analysis.

Setting: At a single pediatric hospital.

Participants: Fourteen pediatric patients with failing SV physiology receiving ventricular assist device therapy (SVAD).

Interventions: None.

Measurements and Main Results: Preoperative, intraoperative, and postoperative patient demographic and medical data were obtained from prior inpatient progress notes, laboratory values, anesthetic records, cardiac catheterization reports, echocardiography reports, and postoperative surgical notes entered during inpatient encounters at the time of SVAD placement. Between April 5, 2010, and December 1, 2020, 16 VAD device implants supported 14 pediatric patients with failing SV physiology. Most patients presented with a preoperative diagnosis of hypoplastic left heart syndrome (N = 9, 64.3%). A total of 6 patients expired on VAD therapy (43%), 7 (50%) survived to receive a cardiac transplant, and 1 patient currently remains on device therapy.

Conclusion: Although our institutional approach represents a single perspective, we anticipate that our experience institutional experience may prove helpful to others caring for peditric patients with single ventricle physiology undergoing ventricular assist device placement and promote collaborative efforts to improve their care.

Key Words: Anesthesia; Single ventricular physiology; Ventricular assist devices (VAD); Pediatric heart transplant

TRANSPLANTATION IN PEDIATRIC PATIENTS represents only 10% of total heart transplants performed worldwide, with only 5% to 10% of those achieved in patients with single-ventricle (SV) physiology.[1,2] With advances in surgical techniques, perioperative care, and improvements in outpatient management, a growing population of pediatric patients with SV palliation require mechanical circulatory support (MCS) as a bridge to transplant. Though establishing successful MCS in patients with SV physiology remains challenging, single-

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ventricle assist device (SVAD) support has emerged as a potential therapeutic option for this growing population. Fortunately, the ability to implement ventricular assist device (VAD) therapy reportedly has resulted in up to a 50% reduction in waitlist mortality in all pediatric patients receiving devices, thereby allowing more patients ultimately to undergo transplantation, with only a modest 25% increase in transplant waiting times (median wait increase from 36-45 days).[3] Despite these advancements, limited data currently exist specifically describing the perioperative characteristics and benefits of implementing SVAD therapy in the subset of patients with SV physiology.

Historically, outcomes for stage I patients requiring VAD support have been poor. Limited reports on pre-Glenn patients with SV anatomy supported on the Berlin Heart EXCOR (Berlin Heart, Inc; The Woodlands, TX) demonstrated decreased survival when compared with patients with post-Glenn or post-Fontan (11% *v* 58% *v* 60%) physiology.[1] Patients with stage II physiology requiring VADs are also a challenging group to support, with 20% to 58% of patients surviving to transplant or recovery in small case series.[1-3] Unfortunately, distinct postoperative outcomes, including overall mortality and subsequent transplantation rates, in the SV population, rarely are distinguished from other VAD recipients with congenital heart disease (CHD) with biventricular physiology.[4] Addressing this limitation requires a focused distinction among unique CHD subsets to bridge the understanding of how patient characteristics and perioperative management may influence outcomes in patients with SV physiology. This report presents a retrospective case series describing the detailed characteristics and outcomes of patients with failing SV physiology undergoing VAD placement at a high-volume pediatric VAD center. Within this cohort, the implantation of 16 devices in 14 pediatric patients with SV physiology occurred between April 5, 2010, and December 1, 2020. The authors believe that sharing their institutional experience provides further insight to help guide future management and perioperative care in these patients.

Definitions

With regard to institutional VAD volume, *high-volume* was defined according to the Pediatric Interagency Registry for Mechanical Circulatory Support (Pedimacs) definition, which included centers enrolling ≥15 VAD patients within approximately 5 years (ie, between September 19, 2012, through June 20, 2017).[4] In most instances, the term *biventricular assist device* (BiVAD) may not provide an accurate clinical description when 2 devices may be required to support patients with SV physiology. For this study, VAD or SVAD denotes a device implanted into the systemic ventricle (or adjacent atrium), regardless of the underlying morphology. However, in unique circumstances, 2 devices may be warranted to independently support both the failing systemic ventricle and the cavopulmonary venous system (ie, circulatory failure). A cavopulmonary augmentation device (CAD) may be incorporated into the total cavopulmonary anastomosis (TCPA) at the time of initial SVAD placement.[5] Mechanically-assisted Fontan completion is a relatively new approach for the failing Glenn circulation due to isolated univentricular dysfunction in Fontan-eligible age.[6] During this procedure, TCPA is completed concomitantly with VAD implantation to minimize the deleterious effects of persistent cyanosis.

Methods

After Institutional Review Board approval, a retrospective chart review was performed for all patients with failing SV physiology receiving VAD therapy between April 5, 2010, and December 1, 2020, using institution-based electronic medical records. Patients were identified using the electronic medical record reporting system to include all cardiothoracic surgical patients undergoing procedures in both operative and hybrid surgical locations. The report criterion was further specified by the following procedure types: cardiac BiVAD placement, cardiac left VAD placement, cardiac VAD placement, LVAD versus BiVAD Berlin Heart, and Impella VAD (ABIOMED). All collected data were verified by 2 physician-investigators independently. The final statistical analysis used preoperative, intraoperative, and postoperative data obtained from prior inpatient progress notes, laboratory values, anesthetic records, cardiac catheterization reports, echocardiography reports, and postoperative surgical notes entered during inpatient encounters at the time of SVAD placement. Patient demographic and clinical variables reflected the frequency (%) for categorical and mean ± SD or median with interquartile range (IQR) for continuous variables. Patients were censored when they met a study endpoint defined as death, transplant, recovery, or cessation of support.

Results

Preoperative SVAD Patient Characteristics

Between April 5, 2010, and December 1, 2020, 16 VAD device implants were placed in 14 pediatric patients with failing SV physiology. A total of 6 patients expired on VAD therapy (43%), 7 (50%) survived to receive a cardiac transplant, and 1 patient currently remains on device therapy. Of these patients, 6 (42.9%) were female. Most patients presented with a preoperative diagnosis of hypoplastic left-heart syndrome (n = 9, 64.3%) before device implantation. Preoperative cardiac diagnoses additionally included pulmonary atresia with an intact ventricular septum (PA-IVS) in 2 patients (14.3%), and mixed, complex cardiac conditions in the remaining 3 (21.4%). At device placement, stage II palliation (n = 8, 57.14%) was the predominant preoperative anatomic configuration. One patient (7.1%) was classified as pre-Glenn, whereas 5 (35.7%) presented with stage III palliation at the time of implant. The median patient age was 3.85 (IQR) years, with a median body surface area (BSA) of 0.67 m^2 (IQR). More than two-thirds (71.4%) of all patients were intubated on mechanical ventilation at the time of device placement, one-third of whom survived to receive transplantation. Pacemaker

Table 1
Preoperative Patient Chracteristics of all SVAD Patients.

	Preoperative Patient Characteristics												Intraoperative Patient Characteristics						Postoperative Patient Characteristics			
	Postdevice Outcome	Age, y	Original Diagnosis	Weight, kg	BSA, m^2	Cardiac Arrest Preimplant	Cardiac Arrest Occurrence (d Prior to Implant)	ECMO Required Preoperatively	d on ECMO Prior to VAD Insertion	Intubated Prior to VAD Placement	Preoperative Insertion of Peripheral VAD (Impella)	Physiology	VAD Type	SVAD Inflow Cannulation Site	SVAD Outflow Cannulation Site	Cavopulmonary Inflow Cannulation Site	Cavopulmonary Outflow Cannulation Site	Fontan Conversion Intraoperatively	Intraoperative Oxygenator Placed	Postoperative Oxygenator Placed	Support Duration, d	Postoperative Cardiac Catheterization Requiring Vascular Collateral Coiling on VAD	Discharged Home on Device
Patient 1	On VAD	3	HLHS	17	0.67	Yes	7	Yes	7	Yes	No	Hemi-Fontan	PediMag	Ventricular apex	Ascending aorta	TCPA	PA	Yes	No	No	739*	No	No
Patient 2	Transplanted	1.28	HLHS	8.3	0.41	Yes	13	Yes	13	Yes	No	Glenn	PediMag	Ventricular apex	Innominate artery	TCPA	PA	Yes	Yes	Yes	322	Yes	No
Patient 3	Transplanted	7.24	Complex	17.7	0.74	No		No		Yes	No	Fontan	PediMag	Ventricular apex	Ascending aorta	NA		No	No	No	17	No	No
Patient 4	Transplanted	13.43	HLHS	48.9	1.47	No		No		No	No	Fontan	Heartmate 3	Ventricular apex	Ascending aorta	NA		No	No	No	222	Yes	No
Patient 5	Transplanted	9.96	HLHS	29.6	1.05	No		No		No	No	Fontan	Heartmate 3	Ventricular apex	Ascending aorta	NA		No	No	No	142	Yes	Yes
Patient 6	Transplanted	8.82	HLHS	19.1	0.78	No		No		No	No	Glenn	Heartmate 3	Ventricular apex	Ascending aorta	NA		Yes	No	No	244	Yes	Yes
Patient 7	Transplanted	1.33	HLHS	8.7	0.43	No		No		Yes	No	Glenn	PediMag	Ventricular apex	Ascending aorta	NA		No	No	No	33	No	No
Patient 8	Transplanted	6	HLHS	21.8	0.83	No		No		No	No	Fontan	Berlin	Ventricular apex	Ascending aorta	NA		No	No	No	81	No	No
Patient 9	Not transplanted	4.03	PA/IVS	12.9	0.55	No		Yes	16	Yes	No	Glenn	PediMag	Common atrium	Ascending aorta	NA		No	No	Yes	123	No	No
Patient 10	Not transplanted	0.1	PA/IVS	3.6	0.22	Yes	1	No		Yes	No	Pre-Glenn	PediMag	Common atrium	Ascending aorta	NA		No	No	No	55	No	No
Patient 11	Not transplanted	1.04	HLHS	10.2	0.45	Yes	1	Yes	1	Yes	No	Glenn	PediMag	Ventricular apex	Ascending aorta	NA		No	Yes	No	4	No	No
Patient 12	Not transplanted	9	Complex	30.4	1	Yes	4	Yes	3	Yes	Yes	Glenn	HeartWare	Ventricular apex	Ascending aorta	NA		No	No	No	12	No	No
Patient 13	Not transplanted	3.67	HLHS	17.2	0.67	No		No		Yes	No	Glenn	Berlin	Ventricular apex	Ascending aorta	NA		No	No	No	271	No	No
Patient 14	Not transplanted	3	Complex	11.85	0.55	No		Yes	3	Yes	No	Fontan	Berlin	Ventricular apex	Ascending aorta	NA		No	No	No	364	No	No

* As of May 1, 2022.Abbreviations: BSA, body surface area; ECMO, extracorporeal membrane oxygenation; HLHS, hypoplastic left heart syndrome; IVS, intact ventricular septum; PA, pulmonary artery; SVAD, single ventricle assist device; TCPA, total cavopulmonary anastomosis; VAD, ventricular assist device.

dependency at the time of device placement was noted in 2 patients (14.3%), both of whom expired before transplant. Preoperative cardiac arrest requiring cardiopulmonary resuscitation occurred in 35.7% of all patients (14.3% of transplanted *v* 50% of expired patients). Preoperative extracorporeal membrane oxygenation (ECMO) was initiated in 42.9% of patients (14.3% transplanted *v* 66.7% expired patients) prior to initial SVAD placement for an average of 7.3 days of ECMO support prior to VAD implant. Of patients requiring preimplant ECMO, 1 transplanted patient and 1 who expired on VAD support required intraoperative oxygenator placement at the time of device insertion. All patients receiving ECMO were transitioned directly to an SVAD intraoperatively except for 1 patient who was transitioned to a percutaneous VAD (ie, Impella) 3 days after initial ECMO support. SVAD placement occurred 3 days after Impella placement; this patient expired on day 12 of support. One expired patient required an SVAD oxygenator on postoperative day 6, and 2 subsequent oxygenator exchanges on postoperative days 84 and 105, respectively. One transplanted patient, who required an SVAD oxygenator, additionally underwent 2 subsequent oxygenator exchanges on postoperative days 1 and 16, for a total of 22 days of oxygenator support. No exchanges were required for 1 patient who received 4 days of oxygenator therapy after the SVAD implant. The discontinuation of oxygenator therapy in this patient occurred at the time of the patient's death in the setting of multiorgan failure. Perioperative characteristics of all patients receiving SVADs are summarized in Table 1.

Intraoperative SVAD Patient Characteristics

Patients were supported using both pulsatile (21.4%) and continuous-flow devices (78.6%). Devices included the Berlin Heart EXCOR paracorporeal pulsatile-flow system (21.4%), Heartware (HVAD; Medtronic) intracorporeal continuous-flow system (7.14%), HeartMate 3 (HM3; Abbott) intracorporeal continuous-flow system (21.43%), and PediMag (Abbott) paracorporeal continuous-flow system (50%). Three patients with failing stage II physiology (21.4%) underwent mechanical Fontan conversion at the time of SVAD placement; 2 required additional CAD support. Of the 2 receiving CAD support, 1 required both ventricular and cavopulmonary device support at the time of the initial implant using the PediMag system, whereas the other received an additional cavopulmonary support device 15 days after the placement of their initial systemic ventricular device. The remaining 12 patients received single- device SVAD therapy, 2 of whom were discharged home and managed in an outpatient setting on implantable SVAD therapy until both received transplants. Cannulation strategies for systemic ventricular support favored ventricular apical inflow cannulation to aortic outflow cannulation in 78.6% of patients. Additional systemic SVAD configurations included common atrial (anatomic left atrium) inflow to aortic outflow cannulation (14.3%), although 1 patient required cannulation using ventricular apical inflow with the innominate artery outflow technique. Cavopulmonary SVAD support required conduit inflow to pulmonary artery outflow cannulation techniques in both patients.

Overall, patients surviving to transplantation received between 17 and 322 days of device support (mean of 151 days). Patients expiring before transplantation received between 4 and 364 days of device support, for an average of 138.2 days of support. One patient currently remains on VAD support and has been supported for more than 739 days as of May 1, 2022.

All but 2 patients receiving VAD support required intraoperative cardiopulmonary bypass (CPB) at the initial VAD placement. Of the patients requiring CPB, 7.14% required a second bypass run, and 14.3% required 3 bypass runs. Both patients who did not require CPB received PediMag devices. In 1 of these patients, the cannulation strategy used was a preexisting aortic outflow ECMO cannula, but received a common atrial inflow cannula insertion at SVAD placement. The second patient underwent apical ventricular inflow cannulation using induced fibrillation with an aortic outflow cannula placed at SVAD insertion. Mechanically-assisted Fontan completion occurred in 3 patients (21.4%) who ultimately received a transplant. Two patients required intraoperative oxygenator placement, 1 of whom required an additional cavopulmonary assist device 15 days after the initial device placement. One patient required postimplant oxygenator therapy after the SVAD implant.

Overall, 78.6% of patients required intraoperative administration of packed red blood cells (PRBCs), 42.9% received fresh frozen plasma, 35.7% received cryoprecipitate, and 71.4% received platelets. Perioperative variables, including blood product administration (mL/kg), are summarized in Tables 2 and 3.

Postoperative SVAD Patient Outcomes of All Patients

Postoperatively, 71.4% of patients required additional blood product administration (42.9% of transplanted patients, 100% of expired patients). Patients received an average of 25.26 ± 33.54 mL/kg of PRBCs, 0.25 ± 0.83 mL/kg of cryoprecipitate, 5.01 ± 7.69 mL/kg of fresh frozen plasma, and 11.58 ± 25.63 mL/kg of platelets in the first 24 hours postimplant. Median

Table 2
Analysis of Preoperative and Postoperative Patient Characteristics and Laboratory. Studies of All Patients Receiving Single-Ventricle Assist Devices.

	Mean	Median	SD	IQR - 25	IQR - 75
Age at implant, y	5.14	3.85	4.02	1.32	8.87
BSA, m^2	0.7	0.67	0.32	0.45	0.87
Preoperative creatinine	0.72	0.7	0.37	0.4	0.92
POD 1 creatinine	1.02	0.85	0.64	0.57	1.33
Delta creatinine	53.87	33.93	75.4	3.17	101.04
Preoperative AST	260.38	67	642.56	37	111.5
POD 1 AST	328.08	205.5	384.87	149.75	291
Delta AST	308.49	153.71	343.74	100.24	676.84
Preoperative ALT	171.15	35	470.96	24	68.5
POD 1 ALT	145	37.5	346.02	30	71.5
Delta ALT	40.9	7.17	125.42	-25.9	39.45
Delayed sternal closure, d	6.57	2	9.73	2	8

Abbreviations: ALT, alanine aminotransferase; AST, aspartate transaminase; BSA, body surface area; IQR; interquartile range; POD, postoperative day.

Table 3
Analysis of Intraoperative Time Intervals and Blood Product Administration of All Patients Receiving Single-Ventricle Assist Devices.

	Mean	Median	SD	IQR - 25	IQR - 75
Duration of anesthesia	525	562	193	401	668
Surgical time	368	351	157	278	447
CPB, min	138	101	101	64	217
Total intraoperative PRBC, mL/kg	18.95	19.11	15.45	8.03	26.39
Total cryoprecipitate, mL/kg	2.01	0	3.61	0	3.79
Total fresh frozen plasma, mL/kg	6.4	0	9.45	0	14.37
Total platelets, mL/kg	14.2	13.58	14.64	0	20.34

Abbreviations: CPB, cardiopulmonary bypass; IQR, interquartile range; PRBC, packed red blood cells.

chest tube output within 24 hours was 3.05 (IQR) mL/kg/h for all patients. Postoperative variables, including blood product administration (mL/kg), are summarized in Table 3. On average, patients undergoing transplantation tended to be older (mean of 6.17 *v* 3.47 years), weighed more (mean of 20.29 *v* 12.38 kg), had a higher BSA (mean of 0.77 *v* 0.57 m^2), and were supported longer (mean of 171 *v* 138.17 days) on device therapy when compared to patients not receiving transplants. Overall, these patients additionally received fewer intraoperative blood products (ie, PRBCs, cryoprecipitate, and platelets) at the time of device placement (Table 5), and had less chest tube output in the first 24 hours postoperatively (mean of 5.83 v 40.94 mL/kg) compared to nontransplanted patients. More than half (57.14%) of these patients did not require blood products in the immediate 24-hour postoperative period, whereas all patients not receiving a transplant required products (Tables 3 and 4).

After device implantation, 21.4% (n = 3) of patients experienced radiologically confirmed neurologic events within 30 days of device implant. One patient developed pericardial effusion on postoperative day 9, requiring a pericardial window, whereas another patient developed an acute episode of hematemesis/hemoptysis on postoperative days 16 and 23, requiring esophagogastroduodenoscopy and nasal endoscopy without intervention. Most patients (57.1%) underwent delayed sternal closure after device insertion (2.0 days, 6.57 ± 9.73 days).

Table 4
Analysis of Postoperative Chest Tube Output and Blood Product Administration.

	Mean	Median	SD	IQR - 25	IQR - 75
Chest tube output in first 48 hours, mL/kg/h	14.86	3.05	48.96	1.05	6.81
PRBCs transfused within first 24 hours, mL/kg	25.26	15.04	33.54	0	49.81
Cryoprecipitate transfused within first 24 hours, mL/kg	0.25	0	0.83	0	0
Fresh frozen plasma transfused within first 24 hours, mL/kg	5.01	0	7.69	0	10.88
Platelets transfused within first 24 hours, mL/kg	11.58	8.33	25.63	0	14.12

Abbreviation: IQR, interquartile range; PRBCs, packed red blood cells.

Perioperative Device Complications

Three patients who did not survive to transplant required device exchanges (2 Berlin EXCOR devices and 1 PediMag device). Reasons for device exchange included ongoing hemolysis in 1 patient after 22 days of PediMag support, device upsizing in 1 Berlin device, and clotting in another patient supported with a Berlin EXCOR on 5 separate occasions. One patient surviving to transplant required 3 circuit and 3 connector exchanges while on biventricular SVAD support secondary to fibrin deposits. Device connector exchanges for this patient occurred on postoperative days 57, 70, and 82, whereas device circuit exchanges occurred on postoperative days 41, 57, and 70. Device driver replacement was required in 1 patient supported with a Berlin Heart device.

Discussion

Device Selection

The Fifth Annual Pedimacs Registry Report has detailed the experience of all 1,011 pediatric patients (<19 years of age) receiving 1,229 devices at 47 North American hospitals between September 19, 2012, and December 31, 2020. Only 253 (2%) represented patients with CHD, of whom 161 patients (63.6%) had univentricular anatomy.[6] The authors' practice has reflected a slight increase in the use of implantable continuous-flow (ICF) devices (35.7%) compared to pulsatile devices (21.4%). Historically, pulsatile devices, such as the Berlin EXCOR, addressed the inherent anatomic limitations of smaller patients with a BSA of 0.6 m^2 or less.[7] Despite its advantages, major adverse events, such as thrombosis (50%), infection (50%-70%), bleeding (40%-80%), and neurologic complications, have been reported, leading to mortality in 30% of patients.[8] Additionally, the ability to fully rehabilitate patients using pulsatile devices during long-term support imposes a significant limitation to their clinical use. The improvements in durability provided by ICF devices allowed 2 patients within this study to be discharged home on their HM3 devices while awaiting transplant.

After the discontinuation of the HVAD from production, HM3 is currently the only available United States Food and Drug Administration-approved durable ICF device, recently demonstrating better survival and lower rates of adverse neurologic events in adults.[9] In this study, 3 patients received HM3 devices, all of whom survived until cardiac transplantation. At the time of device implantation, 3 patients presented with failing Fontan physiology and 1 with failing Glenn physiology. Despite the authors' success in using the HM3 for SVAD support, a major limitation of the widespread use of the HM3 in pediatric patients is the device size. Patients <25 kg may need preimplantation fit testing with the aid of axial imaging

Table 5
Transplanted *v* Non-transplanted SVAD Patient Characteristics.

Transplanted SVAD Patient Characteristics													
	Time on VAD to Transplant, d	Age at Implant, y	Weight at Implant, kg	Preoperative Calculated BSA, m^2	Total PRBC Administered Intraoperatively, mL/kg	Total Cryoprecipitate Administered Intraoperatively, mL/kg	Total FFP Administered Intraoperatively, mL/kg	Total Platelets Administered Intraoperatively (cc/kg)	Chest Tube Output in First 24 Hours, cc/kg/h	PRBCs Transfused Within First 24 h, cc/kg	FFP Transfused Within First 24 h, cc/kg	Platelets Transfused Within First 24 h, cc/kg	Cryoprecipitate Transfused Within First 24 h, cc/kg
Mean	171	6.17	20.29	0.77	17.23	0.95	6.04	8.49	5.83	8.75	4.29	3.75	0.38
Median	182	6.62	18.35	0.76	11.51	0	3.9	6.66	1.86	0	0	0	0
SD	120.08	4.57	13.82	0.37	19.37	1.7	7.37	9.2	9.99	18.27	7.37	6.44	0.99
Range	305	12.15	40.6	1.06	56.23	4.22	18.87	21.28	27.57	48.84	16.32	14.12	2.63
Minimum	17	1.28	8.3	0.41	0	0	0	0	0.5	0	0	0	0
Maximum	322	13.43	48.9	1.47	56.23	4.22	18.87	21.28	28.07	48.84	16.32	14.12	2.63

Non-transplanted SVAD Patient Characteristics													
	Time on VAD to Death	Age at Implant, y	Weight at Implant, kg	Preoperative Calculated BSA, m^2	Total PRBC Administered Intraoperatively, mL/kg	Total Cryoprecipitate Administered Intraoperatively, ml/kg	Total Fresh Frozen Plasma Administered Intraoperatively, mL/kg	Total Platelets Administered Intraoperatively, cc/kg	Chest Tube Output in First 24 h, option = cc/kg/h	PRBCs Transfused Within First 24 h (Option= cc/kg	FFP Transfused Within First 24 h, option = cc/kg	Platelets Transfused Within First 24 h, Option = cc/kg	Cryo Transfused Within First 24 h, option = cc/kg
Mean	138.17	3.47	14.36	0.57	40.25	2.98	4.93	14.11	29.49	40.94	4.41	9.72	0
Median	89	3.34	12.38	0.55	32.78	0	0	15.6	6.62	41.99	0	9.07	0
SD	148.13	3.11	9.02	0.26	30.09	5.22	8.22	9.04	38.83	30	7.17	10.97	0
Range	360	8.9	26.81	0.78	85.23	12.79	19.59	25.49	85.93	66.44	16.67	29.99	0
Minimum	4	0.1	3.6	0.22	12.4	0	0	0	0.99	5.26	0	0	0
Maximum	364	9	30.4	1	97.63	12.79	19.59	25.49	86.92	71.7	16.67	29.99	0

Abbreviations: BSA, body surface area; FFP, fresh frozen plasma; PRBC, packed red blood cells; SVAD, single-ventricle assist devices; VAD, ventricular assist device.

reconstruction either virtually or with 3-dimensional printing to determine fit.[10,11]

Cannulation Strategy

Cannulation strategies for systemic ventricular support favored ventricular apical inflow cannulation over aortic outflow cannulation in 78.6% of patients. Additional systemic SVAD configurations that were used less commonly included common atrial (anatomic left atrium) inflow-to-aortic outflow cannulation (14.3%) and ventricular apical inflow with innominate artery outflow cannulation (7.1%). Proximal innominate artery outflow cannulation site was selected in 1 patient due to insufficient space among the upper extent of the neoaortic valve, arterial cannula, and innominate artery takeoff to enable anastomosis of the outflow graft onto the ascending aorta. When anatomically feasible, the authors' recent practice has favored the placement of a ventricular inflow cannula to improve the mixing of deoxygenated and oxygenated blood and the efficiency of ventricular decompression. Inflow cannulation within the ventricular apex additionally improves the pressure gradient across the outflow for an extended period while preserving native cardiac output in the setting of sudden increases in afterload.[3]

Device Support for Failing Stage I Palliation

The support of stage I SV-CHD circulation is challenging due to multiple factors. These include small patient size, limited support options, immaturity of the coagulation system, and the nature of a parallel circulation with the nearly unavoidable imbalance between systemic cardiac output and pulmonary blood flow due to the dropping pulmonary vascular resistance.[12,13] An analysis performed using the Pedimacs Registry described the outcomes of 23 patients with stage I physiology on SVAD support using Pedimacs data.[4] Of the 23 patients, 10 patients (43%) died, with the median survival on VAD being just <3 months after implant. Of these patients, 74% were <12 months old, highlighting the challenges of size, immaturity, and fragility. Additionally, poor outcomes may have been attributable to their preimplant clinical status; 13 of 23 (59%) were Interagency Registry for Mechanically Assisted Circulatory Support (INTERMACS) profile 1, and 7 of 23 (30%) were on ECMO prior to VAD implantation.

The authors' singular patient with stage I physiology (PA-IVS with right ventricular-dependent coronary circulation [RVDCC]) similarly reflected challenges related to preimplant clinical status, small patient size, and immaturity. Patients with PA-IVS and RVDCC represent a particularly challenging subset of neonates requiring VAD placement. The presence of coronary ostial atresia creates a reliance on retrograde filling from ventricular fistulae providing bidirectional (ventricular wall-to-patent intramural coronaries) flow, predisposing the myocardium to ischemic events exacerbated by ventricular decompression (ie, SVAD placement). For these reasons, periods of low cardiac output and decreased systemic oxygen delivery also may exacerbate the incidence of severe ventricular infarction in the postoperative period. In these instances, intraoperative myocardial protective strategies during device implantation may be required for improved outcomes after the VAD is initiated. For these reasons, common atrial inflow cannulation (ie, Sondergaard's groove within the left atrium) represented a less commonly employed support strategy in patients with PA-IVS to avoid relying on an atrial septal defect to enable the adequate drainage of pulmonary venous return. Implementing a left atrial inflow cannulation strategy provides the potential advantage of being performed without bypass and, therefore, without right atrial and right ventricular decompression risking coronary ischemia.[14] Additionally, the risk of dislodging the stents maintaining ductal patency (eg, patients with PA-IVS with RVDCC previously undergoing ductal stent placement) by lifting the ventricular apex to perform apical cannulation is avoided. In the event of myocardial infarction and necrosis, atrial cannulation would be less likely to dehisce, and the potential to maintain some pulsatility might minimize the risk of excess pulmonary blood flow. This patient received 55 days of device support before developing mycobacterial bacteremia leading to multiorgan failure and, ultimately, death prior to receiving transplantation.

Device Support for Failing Stage II Palliation

One complication distinctive to patients with Glenn physiology after VAD implantation is the risk for potentiating preexisting cyanosis, either from inadequate mixing with right-to-left shunting from the inferior vena cava in the setting of atrial inflow cannulation or from venovenous collaterals.[5,15] Although a VAD may result in improved cardiac output and adequate decompression of the systemic ventricle, it does not necessarily protect against circulatory failure and may even aggravate venous hypertension. Although stage-II patients benefit from a stable source of pulmonary blood flow in series after the cavopulmonary anastomosis and aortopulmonary shunt division, the adequacy of passive upper body venous return becomes compromised from the development of acquired venous collaterals over time. Over time, volume overload from extensive venous collateralization may exceed the ability of an SVAD to generate sufficient flows that provide adequate ventricular decompression without risking extensive hemolysis. At the authors' institution, half of all patients who ultimately received a transplant required postoperative coiling of collateral vessels in the cardiac catheterization suite; whereas patients not surviving to transplant, did not receive transcatheter interventions. Identifying and limiting the venous decompression required for optimal VAD support via preoperative or postoperative collateral coiling may provide a practical intervention to improve support strategies.

As previously stated, despite adequate decompression within the systemic circulation, the superior cavopulmonary venous circulation may remain congested due to a reliance on passive return to the pulmonary arteries. Even though increased systemic output and decompression of the systemic ventricle can result in improved hemodynamics and improved superior cavopulmonary connection (SCPC) return, patients supported with a VAD after stage-II palliation still may

experience discrepancies in systemic venous decompression between the upper and lower body, with persistent SCPC congestion. In addition to inadequate decompression, progressive cyanosis from the formation of collateral vessels can contribute to subsequent pleural effusion development in a failing Glenn circulation that is unable to keep up physiologically with the increased cardiac output generated from the VAD.

Various strategies have emerged to address worsening cyanosis after stage-II VAD implantation, with some patients being reverted to stage-I circulation with the takedown of the SCPC and the creation of an aortopulmonary connection.[16] Generally, older stage-II patients with a higher BSA may instead undergo conversion to stage-III physiology ("mechanically-assisted Fontan completion") at the time of SVAD implantation.[6,17,18] Despite their opposing directions, both approaches resolve the dichotomous systemic venous return, which remains a fundamental problem with the stage-II SVAD. In a salvage situation, Glenn takedown with shunt conversion may have to be undertaken in smaller infants shortly after the Glenn surgery (ie, early Glenn failure). However, older patients who deteriorate gradually with failed Glenn circulation due to systemic ventricular dysfunction may benefit from the Fontan completion strategy (ie, late Glenn failure).[3] This strategy is consistent with the natural progression of the SV palliation (ie, total cavopulmonary connection) rather than the return to a shunted state. Given the substantial outcome differences between the stages I and III SVAD cohort, cumulative institutional experience makes it increasingly challenging to justify the shunt strategy when the patient is a reasonable candidate for Fontan completion strategy. As the benefits of augmenting cardiac output with a stage-II VAD become negatively offset by worsening hypoxia,[19] performing a mechanical Fontan conversion improves not only cardiac output (with SVAD) but also systemic arterial oxygen saturations (from <80% to nearly 100%), leading to combined improvement in oxygen delivery capacity, which is the fundamental goal in heart failure management.[20] In the authors' experience, these benefits become particularly salient when the scope of VAD support is not just a relatively short-term bridge to transplant, but rather chronic, durable support that may be required for months to years.[21]

The authors' practice also has incorporated the use of cavopulmonary mechanical support devices (ie, TCPA inflow to pulmonary artery outflow cannulation strategy) in converted patients with increased pulmonary vascular resistance to address persistent hypoxia and limit systemic venous congestion. This method of support decompresses the congested systemic venous system by mechanically assisting passive pulmonary blood flow that cannot be achieved with isolated systemic SVAD therapy alone.[22]

Ultimately, the inconsistencies in outcomes data for patients with stage-II SV receiving SVAD therapy likely were a result of the heterogeneity among patients because of different etiologies of SCPC failure (ie, early failure *v* late failure; impaired ventricular function *v* circulatory failure), highlighting the need for an individualized assessment of the mode of failure and the ideal mode of mechanical support.[5]

Device Support for Failing Stage III Palliation

After stage-III palliation, patients can present with isolated systolic ventricular failure but additionally may develop circulatory dysfunction characteristic of failing Fontan physiology. This unique variety of Fontan failure presents a unique constellation of problems, including plastic bronchitis, protein-losing enteropathy, hepatic congestion, and ascites with preserved ejection fraction. SVAD support has been used successfully in the Fontan population for isolated systemic ventricular dysfunction with normal pulmonary vascular resistance. However, the mechanism of Fontan failure may be multifactorial, involving complex interactions among the ventricle, pulmonary vascular bed, and venous compartment. Systemic venous hypertension related to the latter 2 may warrant cavopulmonary support. An isolated systemic device in this setting cannot achieve adequate pulmonary venous decompression in a system reliant on passive flow, and may not improve the signs and symptoms of Fontan circulatory failure. For these reasons, the authors' institutional practice has favored the implementation of an additional cavopulmonary support device in addition to the SVAD to successfully augment pulmonary blood flow. This method individually treats both etiologies of heart failure as distinct entities by providing the ability to independently optimize the loading conditions imposed by each component of mixed-Fontan failure (ie, failing total cavopulmonary circulation and systemic ventricular dysfunction).

Perioperative Characteristics of SVAD Patients

In this study, several potential patient characteristics were associated with worse postoperative outcomes after device insertion. These characteristics included the requirement for preoperative mechanical ventilation, pacemaker dependency prior to initial VAD placement, cardiac arrest within a week of device placement, and pre-SVAD ECMO requirement. Although two-thirds of all patients required mechanical ventilation at device placement (71.4%), only 21% survived to receive transplantation. Pacemaker dependency was noted in 2 (14.3%) patients, both of whom did not survive until cardiac transplant. Historically, patients with earlier stages of failing SV physiology (particularly stages I and II) were more likely to be treated with VADs as *salvage* therapy (ie, patients in critical cardiogenic shock) as defined by the INTERMACS profile.[23]

In this regard, relatively poor survival outcomes are not totally unexpected as a natural consequence of device placement in the most tenuous patients (ie, smaller infants and neonates with complex physiology). Similarly, patients in the authors' study receiving VAD placement within 1 week of experiencing a cardiac arrest exhibited poorer outcomes. For this reason, distinguishing between *elective* and *salvage* strategies becomes critical, as significant outcome improvements may be achieved when an earlier primary elective approach is employed.[24] The inherent risks imposed by ECMO therapy at the time of cardiac arrest are compounded by VAD therapy. Extracorporeal cardiopulmonary resuscitation (ECPR) significantly affects survival to discharge,

with survival rates reportedly ranging between 36% to 42%.[25,26] Though univentricular heart disease has not been associated with increased mortality after ECPR, significant neurocognitive morbidity incurred from ECPR alone may be exacerbated further in the presence of a VAD.

Of those patients experiencing preoperative cardiac arrests, 1 pre-Glenn patient with PA-IVS and RVDCC experienced a bradycardic arrest 1 day prior to VAD insertion. A second patient, presenting with hypoplastic left-heart syndrome with mitral atresia, aortic stenosis, and Glenn physiology, experienced a bradycardic arrest during intubation for respiratory arrest 1 day prior to the initial VAD insertion. At the time of arrest, the patient was placed emergently on ECMO for cardiopulmonary support. Support was withdrawn 4 days after VAD placement due to severe neurologic global ischemia from a prior arrest. A third patient additionally experienced an episode of bradycardic arrest while obtaining vascular access in the cardiac catheterization laboratory. This patient was a 9-year-old male patient with a complex cardiac history significant for transposition of the great arteries, unbalanced atrioventricular septal defect with hypoplasia of the left ventricle, total anomalous pulmonary venous connection with obstruction, visceral heterotaxia, and asplenia with Glenn physiology.

Timing of VAD) Placement

Critical to the successful deployment of VAD support is the process of timely and thoughtful evaluation. However, the ideal timing of a durable assist device implantation in patients with end-stage heart failure presenting with INTERMACS profile 1 is still controversial. The practice of implementing SVAD support as rescue therapy in failing patients with SV physiology requiring ECMO has diminished with growing institutional experience, limiting VAD candidacy in those who cannot wean off ECMO.[3] The data on extracorporeal life support as a bridge to VAD are limited, with adult studies observing a high incidence of acute kidney injury on dialysis (68.6%), and respiratory failure (77%) in a majority of patients with acute cardiogenic shock.[27] The intraoperative and postoperative coagulopathy observed in the authors' data may correlate to similar clinical manifestations of end-organ damage after extracorporeal life support that potentially predispose patients to an increased need of perioperative blood products and increased bleeding in the postoperative period after VAD placement.

Institutional success implementing chemical hybrid strategies (ie, prostaglandin infusion and bilateral pulmonary artery bands for ductal-dependent systemic circulation) suggest another potential approach for improving the chances of receiving a heart transplant[3] in patients at heightened risk for myocardial ischemia after ventricular decompression with SVAD therapy (ie, PA-IVS and right ventricular-dependent coronary perfusion). Using this approach for stage-II patients, Puri and Adachi described their favorable institutional experience supporting 10 patients with Glenn physiology with a VAD, of whom 90% went on to receive heart transplantation. Of the 4 patients in this cohort who remained in stage-II physiology after VAD implantation, only 1 (25%) remained intubated until heart transplant, and none required an oxygenator while on VAD support.[3]

There are no consensus guidelines on managing patients with SV physiology on a VAD to improve outcomes. Although small patients can do well with proper patient selection, infants with univentricular physiology pose additional anatomic and physiologic challenges, resulting in less-favorable outcomes than other pediatric populations. SV physiology represents a common pathway encompassing a very heterogeneous and complex group of patients. Personalized medicine is the mainstay of care in SV patients, and the same consideration applies when considering how and when to best use MCS.[28]

Device Selection

A final consideration is device selection, particularly concerning the type of VAD (ie, pulsatile *v* continuous flow [CF]). Although pulsatile and CF devices can decompress the heart adequately, computational studies examining pulsatile flow devices have demonstrated an inability to maintain the higher cardiac output requirement associated with parallel circulation, such as that with a systemic-to-pulmonary shunt.[29] Paracorporeal CF centrifugal devices address the dynamic flow requirements associated with SV physiology, as well as the expected decreases in pulmonary vascular resistance occurring within the neonatal period. Furthermore, the additional flow requirements associated with the acute postbypass period are better addressed with CF devices. Rather than providing a fixed output, centrifugal devices acclimate to variations in vascular resistance, providing a more stable support strategy in the acute postoperative period. In addition, recent reports have highlighted the ability of CF devices to generate higher flows at lower filling pressures compared with pulsatile systems. The authors' earlier experience using the Berlin pulsatile pump reflected similar suboptimal outcomes of prior published series, suggesting a potential limitation in the ability to accurately predict the adequate amount of flow required.

Limitations

The descriptive data presented within the study rely on the assumption that documentation within medical records accurately reflect a comprehensive and quantitative account of each patient's admission.

Significant limitations to the authors' study analysis included a smaller patient sample size given the patient population. Center-to-center variability regarding the management of patients with SV physiology, coupled with a lack of standardized management guidelines, limit the accuracy and completeness of the reporting. With only a few patients reviewed, the authors' study and subsequent analysis primarily are descriptive. The current lack of available preexisting data and sufficient patient population, limit the derivation of meaningful clinical recommendations. Similar to results reported by the Pedimacs analysis, the heterogeneity of this smaller patient population prevented adequate decoupling of the effects of

age, size, and device. Calculations presented were limited by reliance on the assumption that documentation within medical records accurately reflected the data presented in this study.

Conclusion

Patients requiring SVADs present multifaceted and unique perioperative challenges that require a definite command over a myriad of complex congenital cardiac lesions. Improvements in surgical palliation that have led to increased patient longevity present an opportunity to explore and develop optimal patient pathways during this era of MCS. Despite providing a long-term management option for these complex SV patients, an increased risk for significant hemodynamic bleeding, clotting, infectious complications, and embolic events that would preclude transplantation exists. Due to sensitization from repeated blood exposures both before and after VAD implantation, waitlist times may be prolonged. In this manuscript, the authors presented their perioperative institutional experience and outcomes in patients with SV physiology requiring SVAD therapy. Although they understand that their institutional approach represented a single perspective, the authors anticipate that their experience at a high-volume VAD institution may prove helpful to others caring for this unique subset of patients and promote collaborative efforts to improve care. A better understanding of patient demographics, device selection, and response to anesthetics is essential for safe care for these children.

Conflict of Interest

None.

Supplementary materials

Supplementary material associated with this article can be found in the online version at doi:10.1053/j.jvca.2022.06.038.

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