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Pulmonary artery pulsatility index predicts prolonged inotrope/pulmonary vasodilator use after implantation of continuous flow left ventricular assist device

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Abstract

Objective: Predictors of right ventricle (RV) dysfunction after continuous-flow left ventricular assist device (CF-LVAD) implantation in children are not well described. We explored the association of preimplantation Pulmonary Artery Pulsatility index (PAPi) and other hemodynamic parameters as predictors of prolonged postoperative inotropes/pulmonary vasodilator use after CF-LVAD implantation.

Design: Retrospective chart review.

Setting: Single tertiary care pediatric referral center.

Patients: Patients who underwent CF-LVAD implantation from January 2012 to October 2017.

Interventions: Preimplantation invasive hemodynamic parameters were analyzed to evaluate the association with post-CF-LVAD need for prolonged (>72 hours) use of inotropes/pulmonary vasodilators.

Measurements and main results: Preimplantation cardiac catheterization data was available for 12 of 44 patients who underwent CF-LVAD implant during the study period. Median (IQR) age and BSA of the cohort were 15.3 years (10.2, 18) and 1.74 m^2 (0.98, 2.03). Group 1 (n = 6) included patients with need for prolonged inotropes/pulmonary vasodilator use after CF-LVAD implantation and Group 2 (n = 6) included those without. Baseline demographic parameters, cardiopulmonary bypass time, and markers of RV afterload (pulmonary vascular resistance, PA compliance and elastance) were similar among the two groups. PAPi was significantly lower in group 1 compared to group 2 (0.96 vs 3.6, respectively; P = .004). Post-LVAD stay in the intensive care unit was longer for patients in group 1 (46 vs 23 days, P = .52). Brain natriuretic peptide was significantly higher at 3 months after implantation in group 1; P = .01.

Conclusions: The need for inotropes/pulmonary vasodilators in the postoperative period can be predicted by the preimplantation intrinsic RV contractile reserve as

Abbreviations: BNP, brain natriuretic peptide; CF-LVAD, continuous-flow left ventricular assist device; CVP, central venous pressure; ICU, intensive care unit; iNO, inhaled nitric oxide; LAP, left atrial pressure; LOS, length of stay; PA, pulmonary artery; PAPi, pulmonary artery pulsatility index; PVR, pulmonary vascular resistance; RA, right atrium; RV, right ventricle; RVD, right ventricular dysfunction; RVSWI, right ventricular stroke work index.

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assessed by PAPi rather than the markers of RV afterload. Further investigation and correlation with clinical outcomes is needed.

KEYWORDS
cardiac catheterization, cardiac filling pressure, continuous flow ventricular assist device, hemodynamics, pulmonary artery pulsatility index, right ventricular dysfunction

1 | INTRODUCTION

Continuous-flow left ventricular assist devices (CF-LVAD) have been increasingly used for children with end-stage heart failure commonly as a bridge to heart transplant and occasionally as destination therapy.[1] Some degree of right ventricular (RV) dysfunction is considered to be frequently present at the time of LVAD implantation. It is thought that LVAD support may help in the recovery of the RV function through reduction of left atrial pressure (by decompressing the left ventricle) and thereby decreasing the RV afterload. However, RV failure or dysfunction can persist in 10%-40% patients[2-4] and cause a significant increase in morbidity and mortality.[3,5,6] At present, the diagnosis of RV dysfunction relies on clinical evidence of venous congestion (elevated CVP), clear lung fields, and evidence of low cardiac output (necessitating prolonged inotrope or pulmonary vasodilator therapy for RV support) despite optimal placement and function of the LVAD device. RV dysfunction necessitates prolonged inotrope and pulmonary vasodilator support in the postoperative period, and, in some cases, requires RV assist device (RVAD) implantation.[7] We aimed to identify hemodynamic predictors of prolonged use of pulmonary vasodilators and inotropes after CF-LVAD based on preimplantation invasive hemodynamic cardiac catheterization data.

Previously identified invasive hemodynamic variables shown to correlate with RV dysfunction in adults include elevated right atrial (RA) pressure, elevated cardiac filling pressure ratio (mean RA to mean pulmonary capillary wedge pressure (PCWP) ratio), and reduced right ventricular stroke work index (RVSWI).[8] Pulmonary artery pulsatility index (PAPi) is a simple hemodynamic calculation [(systolic PA-diastolic PA)/mean RA pressure] which was initially studied to predict RV dysfunction in adults after acute inferior myocardial infarction.[9] Subsequent studies have shown that PAPi might be helpful in predicting RVAD after implantation of CF-LVAD devices in adults.[10,11] We hereby evaluated the usefulness of various invasive hemodynamic factors prior to LVAD implantation to predict the need for prolonged use (>72 hours) of pulmonary vasodilators/inotropes in children.

2 | METHODS

In this retrospective study, we reviewed the records of children who underwent CF-LVAD placement at the Heart Center, Texas Children's Hospital and Baylor College of Medicine, Houston, TX from January 2012 to October 2017. The patients who underwent invasive hemodynamic assessment using cardiac catheterization prior to placement of CF-LVAD were included in analysis. Patients who had single ventricle palliative surgical procedures (Glenn/Fontan operation) were excluded from analysis. Patients who had mechanical or surgical complications post-LVAD (such as significant fluid collections in the pleural, pericardial, or abdominal cavity; surgical site bleeding causing hemodynamic compromise or needing re-exploration) were excluded from the analysis. The study was approved by the Institutional Review Board.

Demographic, clinical, laboratory, and hemodynamic data were reviewed and evaluated for their association with prolonged inotropes and pulmonary vasodilator use. Patients were subcategorized into two groups. Group 1 included those patients who needed inotropes (epinephrine/norepinephrine/vasopressin/milrinone) and pulmonary vasodilators (inhaled Nitric Oxide or intravenous sildenafil) beyond 72 hours after CF-LVAD implantation. Group 2 included those patients who did not need inotropes and pulmonary vasodilators beyond 72 hours of the CF-LVAD implantation. Hemodynamic data (mean RA pressure, pulmonary artery systolic and diastolic pressure, cardiac index, pulmonary/systemic vascular resistance) were obtained from invasive cardiac catheterization data performed prior to placement of CF-LVAD using the Fick principle and incorporating dissolved oxygen content.

Cardiac filling pressure ratio was calculated as the ratio of mean RA pressure to mean PCWP. PAPi was calculated as (systolic PA-diastolic PA)/mean RA pressure. RVSWI was calculated as (mean PA pressure-mean RA pressure) × stroke volume index, where the stroke volume index was calculated as the cardiac index divided by the heart rate. Pulmonary artery compliance was calculated as stroke volume/(systolic PA pressure-diastolic PA pressure). Pulmonary artery elastance was calculated as PA systolic pressure/stroke volume.

All statistical analysis was done using SPSS version 20.0. Continuous variables were expressed as mean ± standard deviation for parametric data, and median (interquartile range) for nonparametric data. Normality was determined using the Shapiro-Wilk test. Qualitative variables were expressed as percentages. Paired Student *t* test (for parametric data) and Wilcoxon-Signed rank test (for nonparametric data) was used for the comparison of different variables. Receiver operator characteristic method was used to evaluate sensitivity and specificity for mean right atrial and cardiac filling pressure values to predict the prolonged use of inotropes and pulmonary vasodilators. Linear and quadratic regression analysis was performed to evaluate pulmonary vascular resistance and other markers of RV afterload (PA elastance and PA compliance). A P value <.05 was considered statistically significant.

3 | RESULTS

Forty-four patients underwent placement of CF-LVAD at our institution during the study period. Invasive hemodynamic assessment prior to placement of CF-LVAD was performed in 15/44 (34.1%) patients (Figure 1). Two patients had undergone single ventricle palliation surgeries prior to CF-LVAD implantation and therefore were excluded from the analysis. One patient developed a large left pleural hematoma causing collapse of the left lung. As the inotrope and pulmonary vasodilator need in this patient was altered by mechanical compression of the lung, the patient was excluded from the analysis (Figure 1).

A total of 12/15 (80%) patients who had invasive hemodynamic measurements prior to placement of CF-LVAD (8 Heartware, HeartWare International Inc., Framingham, Massachusetts and 4 Heartmate-II, Thoratec Corporation, Pleasanton, California) were included in the study. The baseline demographic profile of these patients is shown in Table 1. Median age of the study group was 15.3 years and the median (IQR) interval between the invasive hemodynamic assessment and the CF-LVAD placement was 65 (14, 270) days. The median cardiopulmonary bypass time required for placement of CF-LVAD in the study group was 185 (149, 207.5) minutes.

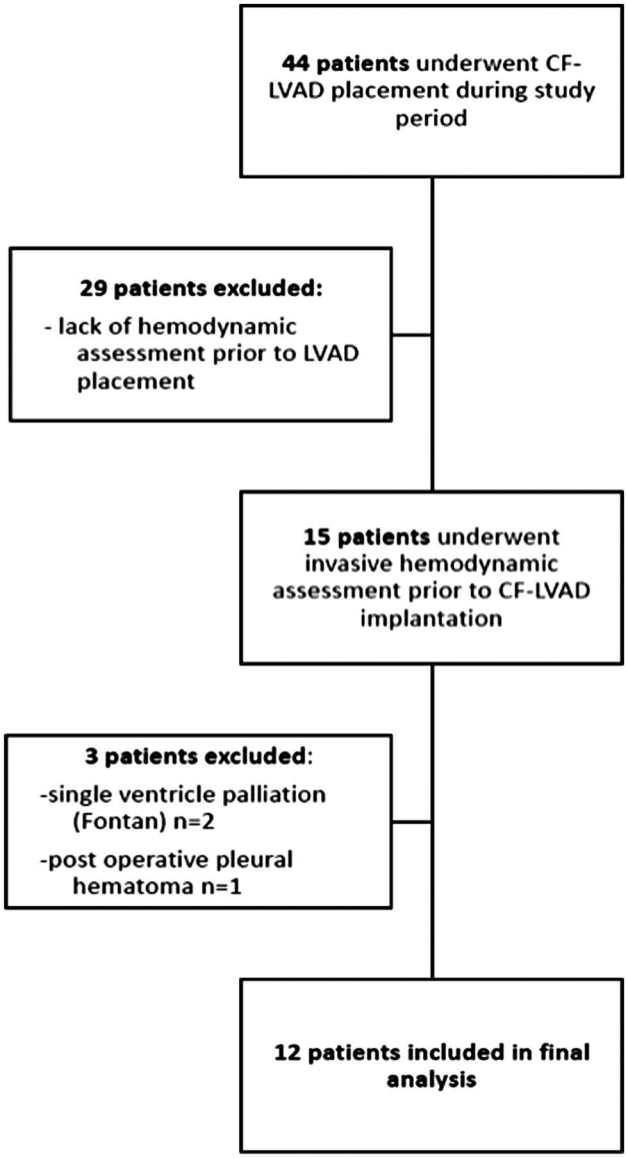

FIGURE 1 Study flow sheet

Majority of the patients had underlying cardiomyopathy (n = 7), four patients had repaired congenital heart disease and one patient had a previous cardiac transplant graft failure. As shown in Table 1, majority of patients underwent placement of CF-LVAD as a bridge to transplant. One patient had a cardiac arrest prior to CF-LVAD placement. Two patients were on mechanical circulatory support prior to CF-LVAD placement and three patients were mechanically ventilated. Baseline serum brain natriuretic peptide (BNP) prior to CF-LVAD implantation was elevated [2169 (983, 2866) pg/mL] in the entire cohort. Patients stayed in the intensive care unit and hospital for a median duration of 35 and 56 days, respectively, after implantation of CF-LVAD.

Various hemodynamic parameters measured at the time of cardiac catheterization in the study group are shown in Table 1. Mean right atrial pressure in the study group was 7 (4.3, 19) mm Hg and other hemodynamic variables and calculated indices are shown in Table 1.

Six patients required prolonged inotrope or pulmonary vasodilators, while the other six did not; and were classified in groups 1 and 2, respectively. The demographic and clinical parameters among these two groups are shown in Table 2. Baseline parameters among patients in the two groups were comparable except for higher pre-LVAD BNP levels among patients in group 2 [2777 (1849, 3169) pg/mL] as compared to patients in group 1 [1442 (640, 2204) pg/mL]; P = .04. Cardiopulmonary bypass time during placement of LVAD was similar in the two groups; P = .87. Post-LVAD stay [median (IQR)] in the intensive care unit [46(5,122) vs 23 (10, 36) days, P = .52] and total hospital length of stay [median (IQR)] was longer in patients in group 1 as compared to group 2 [62(22, 122) vs 51(24.5, 79) days, P = .9]. Though pre-LVAD implantation BNP was higher in group 1, 2 and 3 months post-LVAD BNP was lower in patients in group 2; P = .05 and .01 (Table 2).

Invasive hemodynamic measurements prior to CF-LVAD placement among the two groups are shown in Table 2. Mean RA pressure in group 1 was significantly higher [18 (8.3, 22.3) mm Hg] than patients in group 2 [4.5 (3, 6.5) mm Hg]; P = .008, Figure 2A. Mean pulmonary artery pressures and PCWP were similar in the two groups. Cardiac filling pressure ratio in group 1 was also significantly higher [0.65 (0.42, 0.89)] than patients in group 2 [0.29 (0.19, 0.43)]; P = .016, Figure 2B. PAPi was significantly lower in patients in group 1 [0.96 (0.49, 2.02)] as compared to group 2 [3.6 (3.01, 5.6)]; P = .004, Figure 2C. Other hemodynamic calculations including the pulmonary vascular resistance, pulmonary artery elastance, and compliance were similar in both groups. Patients in group 1 had lower RVSWI than group 2 but this difference did not reach statistical significance; P = .15 (Table 2). Pulmonary vascular resistance significantly correlated with pulmonary artery elastance on linear and quadratic regression analyses, Figure 3.

TABLE 1 Demographic factors of all patients in the study group

Covariate	Study group *n* = 12
Age at VAD implantation, years	15.3 (10.2, 18.01)
Age at cardiac catheterization, years	15.24 (9.54, 17.4)
Catheterization to VAD duration, days	65 (14, 270)
Weight, kg	54.4 (27.7, 80.9)
Height, cm	170 (127.3, 175)
Male, *n*	10 (83%)
Body surface area, m^2	1.74 (0.98, 2.03)
Cardiopulmonary bypass time, minutes	185 (149, 207.5)
Diagnosis	
Failed previous transplant, *n*	1 (8%)
Cardiomyopathy, *n*	7 (58%)
Repaired complex congenital heart disease, *n*	4 (33%)
Ventricular assist device indication	
Destination, *n*	1 (8%)
Bridge to transplant, *n*	7 (58%)
Bridge to candidacy, *n*	4 (33%)
Preoperative mechanical ventilation	
Yes	3 (25%)
No	9 (75%)
Preoperative mechanical circulatory support	
Yes	2 (17%)
No	10 (83%)
Cardiac arrest before VAD	
Yes	1 (8%)
No	11 (92%)
Post-VAD	
Length of ICU stay post-VAD, days	35 (7, 110)
Total hospital LOS post-VAD, days	56 (23, 115)
Total days of invasive ventilation post-VAD	2 (1, 3)
Total support duration, days	427 (120, 785)
BNP (pre-VAD)	2169 (983, 2866)
BNP (1 month)	294 (184, 904)
BNP (2 month)	147 (92, 725)
BNP (3 month)	184 (86, 320)
Hemodynamic characteristics at catheterization (pre-VAD placement)	
Average heart rate, bpm	84.5 (66.5, 117.8)
Mean right atrial pressure, mm Hg	7 (4.3, 19)
Systolic PA pressure, mm Hg	34.5 (27.3, 45)
Diastolic PA pressure, mm Hg	20 (15.3, 25.8)
Mean PA pressure, mm Hg	28 (18.5, 31)
Mean pulmonary capillary wedge pressure, mm Hg	20.5 (14.5, 28)
Mean systemic blood pressure, mm Hg	68 (58.8, 77.5)
Hemodynamic formulas (pre-VAD placement)	
Cardiac filling pressure ratio (mRAP/LAP)	0.43 (0.28, 0.7)
PA pulsatility index, (PAPi)	2.4 (0.8, 3.7)
Pulmonary vascular resistance, $wU.m^2$	2.6 (1.2, 4.6)
Trans pulmonary gradient, mm Hg	6 (2.5, 11.25)
Right ventricular stroke work index	0.44 (0.16, 0.83)
PA compliance, ml/mm Hg	3.9 (1.65, 5.98)
PA elastance, mm Hg/ml	0.16 (0.10, 0.29)

Note: Values reported as "*n*(%)" or median (IQR).
Abbreviations: BNP, brain natriuretic peptide; cm, centimeters; ICU, intensive care unit; kg, kilograms; LAP, left atrial pressure; LOS, length of stay; m, meter; PA, pulmonary artery; PAPi, pulmonary artery pulsatility index; RAP, right atrial pressure; VAD, ventricular assist device.

4 | DISCUSSION

The outcomes of children supported with CF-LVAD continue to gradually improve with growing pediatric VAD experience. RV failure continues to complicate significant number of LVAD implantations and its true physiologic causes remain poorly defined, especially in children. This is the first description of the utility of preoperative invasive hemodynamics in children prior to placement of LVAD as predictors of RV dysfunction as evidenced by the need for prolonged inotropes/pulmonary vasodilators post-CF-LVAD placement in children. We found a lower mean RA pressure, lower cardiac filling pressure ratio and higher PAPi in patients who did not require a prolonged inotropes/pulmonary vasodilator after CF-LVAD placement. The markers of RV afterload were not significantly different among the two groups.

CF-LVAD has become the mainstay in the treatment of end stage heart failure in children. The 2017 PediMACS (Pediatric registry for mechanically assisted circulatory support) registry[12] reports a use of 226 continuous flow devices in children from September 19, 2012 to June 30, 2017 including biventricular assist device use in 5.3% and RVAD use in 1.8% patients. All-cause mortality in this cohort was reported at 10.6%. One of the major causes of the morbidity and mortality after CF-LVAD device placement is RV dysfunction,[11] frequently necessitating prolonged inotrope/pulmonary vasodilator support and intensive care unit stays, and in some cases RVAD support.[6] In our institutional practice, most patients are started on pulmonary vasodilator and inotrope therapy at the time of CF-LVAD implantation on a selective basis. Without supportive clinical evidence of RV dysfunction, we stop inotropes/pulmonary vasodilators within the first 48-72 hours. Therefore, continuation of inotropes and pulmonary vasodilators beyond 72 hours in the postoperative period is an indication of RV dysfunction and can be used as a surrogate of RV dysfunction. Similar to our definition, Soliman et al[13] have previously used a definition

TABLE 2 Various demographic and clinical parameters in patients with and without RV failure/dysfunction

Covariate	Prolonged inotrope/pulmonary vasodilator requirement		
	Group 1, Yes (*n* = 6)	Group 2, No (*n* = 6)	*P* value
Demographic and clinical parameters			
Age at VAD implantation, years	16.1 (13.4, 19.1)	12.6 (8.7, 19.8)	.34
Age at cardiac catheterization, years	15.9 (12.6, 19.1)	12.52 (8.2, 18.8)	.52
Catheterization to VAD duration	34.5 (10.8, 354)	163 (32.5, 361)	.38
Weight, kg	59.5 (41.5, 73.1)	50.3 (19, 86)	.75
Height, cm	170 (157, 175.5)	151.5 (117.5, 177.7)	.52
Body surface area, m^2	1.74 (1.3, 1.8)	1.74 (0.8, 1.8)	.81
Cardiopulmonary bypass time, min	184 (128, 222.3)	185 (159, 232.3)	.87
Length of ICU stay post-VAD, days	46 (5,122)	23 (10, 36)	.52
Total hospital LOS post-VAD, days	62 (22, 122)	51 (24.5, 79)	.9
Total days of invasive ventilation	2.5 (1, 19.8)	1.5 (1, 3.8)	.56
Total support duration, days	145 (82, 182)	709 (223, 1217)	.08
Pre-VAD MCS	1 (16.7%)	1 (16.7%)	1.0
Feeding prior to VAD	4 (66.7%)	5 (83.3%)	.523
Cardiac arrest prior to implant	1 (16.7%)	0 (0%)	.317
Pre-VAD ventilation	2 (33.3%)	1 (16.7%)	.523
BNP (pre)	1442 (640, 2204)	2777 (1849, 3169)	**.04**
BNP (1 month)	607 (172, 965)	245 (184, 610)	.522
BNP (2 month)	725 (253, 895)	94 (88, 321)	**.05**
BNP (3 month)	365 (273, 1156)	105 (59, 163)	**.01**
Hemodynamic characteristics			
Average heart rate, bpm	88 (61.3, 113.3)	84.5 (68.5, 125)	.57
Mean right atrial pressure, mm Hg	18 (8.3, 22.3)	4.5 (3, 6.5)	**.008**
Systolic PA pressure, mm Hg	34.5 (26.5, 50)	35 (26, 49)	.94
Diastolic PA pressure, mm Hg	22.5 (15.8, 30.5)	20 (9.5, 22.8)	.42
Mean PA pressure, mm Hg	28 (19.5, 38.5)	27 (14.8, 31)	.42
Mean PCW pressure, mm Hg	25 (17, 30)	17.5 (10.5, 23.5)	.17
Mean systemic BP, mm Hg	95 (87.3, 102.3)	83.5 (78.3, 100.8)	.23
Hemodynamic formulas			
Cardiac filling pressure ratio, mm Hg	0.65 (0.42, 0.89)	0.29 (0.19, 0.43)	**.016**
PA pulsatility index, (PAPi)	0.96 (0.49, 2.02)	3.6 (3.01, 5.6)	**.004**
PVR, $Wu.m^2$	1.8 (1.08, 4.5)	3.5 (2, 5)	.34
Trans pulmonary gradient, mm Hg	4 (1.5, 10)	7.5 (4, 12.8)	.332
Right ventricular stroke work index	0.29 (0.11, 0.74)	0.49 (0.39, 1.2)	.15
PA compliance	3.9 (1.5, 5.1)	3.5 (1.6, 16.2)	.63
PA elastance	0.21 (0.1, 0.49)	0.13 (0.09, 0.21)	.34

Note: Values reported as N (%) or median (IQR).

Abbreviations: BNP, brain natriuretic peptide; BP, blood pressure; cm, centimeters; ICU, intensive care unit; kg, kilograms; LAP, left atrial pressure; LOS, length of stay; m, meter; MCS, mechanical circulatory support; PA, pulmonary artery; PAPi, pulmonary artery pulsatility index; PCW, pulmonary capillary wedge; PVR, pulmonary vascular resistance; RAP, right atrial pressure; VAD, ventricular assist device.

of iNO ventilation ≥48 hours for early severe right heart failure. Ideally, the RV dysfunction/failure should be defined by poor filling of LVAD despite optimal support. Unfortunately, that information was not available in this retrospective review. However, some support for the use of this cutoff is exhibited by the fact that patients who needed prolonged inotropes/pulmonary vasodilators beyond 72 hours have prolonged ICU and hospital length of stay and significantly higher B-type natriuretic peptide levels after 3 months of CF-LVAD implantation. We excluded patients with single ventricle physiology (Fontan circulation) from this study.

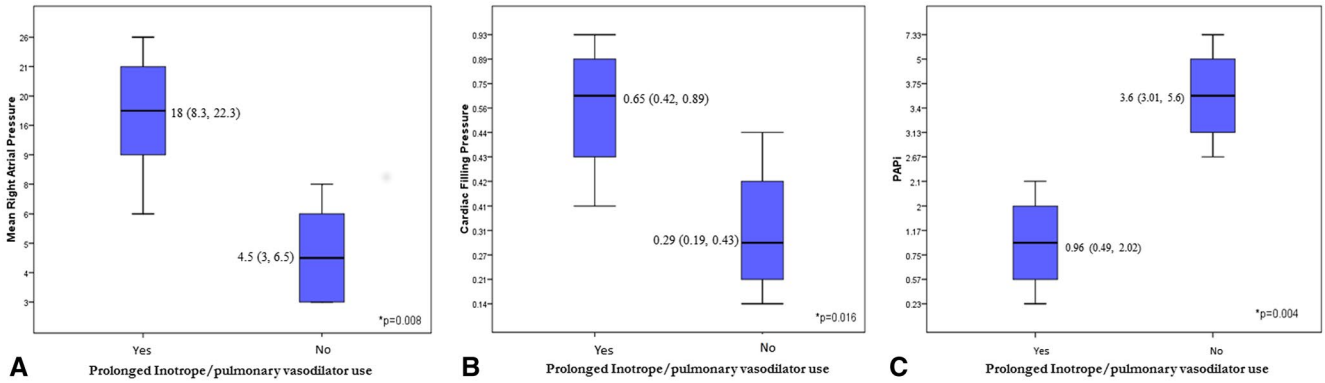

FIGURE 2 Box plot curves showing significantly lower mean right atrial (A) and cardiac filling (B) pressure ratio; and higher pulmonary artery pulsatility index (PAPi) (C) among patients who did not need prolonged inotropes/pulmonary vasodilators after continuous-flow left ventricular assist device placement

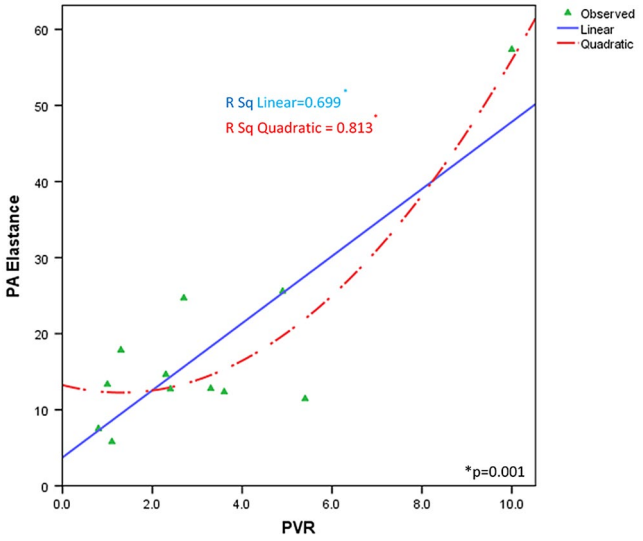

FIGURE 3 Linear and quadratic regression analysis of the PA elastance and pulmonary vascular resistance

This physiology can be considered an extreme end and needs to be evaluated in future studies.

We found that children with prolonged inotrope/pulmonary vasodilator use after CF-LVAD (Group 1) placement had an elevated RA pressure and cardiac filling pressure ratio. Since, the RA pressure interpreted in isolation may be influenced by the volume status, correcting it by dividing with the mean pulmonary capillary wedge pressure (to obtain cardiac filling pressure ratio) gives an estimate of the RV preload with regards to LV preload. We found that cardiac filling pressure ratio in group 1 was significantly higher than patients in group 2 (0.65 vs 0.29; P = .016). Similar to our observation, Lopez-Sendon et al[14] have previously shown cardiac filling pressure ratio >0.86 to be associated with pathological evidence of RV infarction at necropsy. Kormos et al[15] found a pressure ratio of >0.63 associated with RV failure after LVAD placement in adults. The difference in the ratios observed in the above studies could be due to the variability in the measured outcomes.

PAPi is a hemodynamic index used to provide insight into RV preload, afterload, and contractility. The numerator of the index is the PA pulse pressure which may serve as a surrogate marker of RV contractile function and left heart filling pressures as estimated by the PA diastolic pressure. It therefore incorporates the RV pulsatile load as well as the contractile strength. The denominator of the index is the mean RA pressure, which serves as a marker of RV preload and incorporates a marker of RV congestion. Therefore, by combining these parameters into a single index, PAPi provides insight into both RV loading conditions and its mechanics. PAPi was first described by Korabathina et al[16] in adults to identify patients with severe RV dysfunction in acute inferior myocardial infarction. Subsequently, two adult studies[9,10] found PAPi index < 1.85 to be predictive of RV failure after LVAD placement. We provide the first description of the utility of PAPi in assessment of RV function in children. We found a significantly lower PAPi index (0.96 vs 3.6) in patients requiring prolonged inotropes/pulmonary vasodilators after CF-LVAD placement.

Interestingly, the markers of RV afterload like PVR, PA elastance and compliance were not significantly different between the two groups. This is consistent with what has been previously reported and suggests that intrinsic RV contractile reserve rather than the markers of RV afterload determine the need for inotropes/pulmonary vasodilators in the postoperative period.[10] As reported in other studies,[17] we also found a significant positive correlation between PVR and PA Elastance.

The RVSWI calculates RV workload and contractility based on invasive hemodynamics and patient characteristics. Ochiai et al[3] have previously shown that low mean and diastolic pulmonary artery pressures and low RVSWI was significantly associated with RVAD use in adults after LVAD insertion. RV stroke work index < 0.57 gm × m/m^2 is associated with RVF after LVAD placement in adults.[10] We found a higher RVSWI in patients without prolonged need for inotrope/pulmonary vasodilators (0.29 vs 0.49); however, it failed to reach statistical significance (P = .15).

One may question the validity of the study due to the time between catheterization and LVAD placement (median duration of 65 days in our cohort) on the outcomes in a progressive disease. However, Kang et al[10] have shown that time from the right heart catheterization to LVAD placement (1 day-6 months in their cohort) did not change

the predictive ability of the PAPi. The authors concluded that the "hemodynamic changes that identify poor RV response may occur earlier in the disease course than one might expect."[10]

Plasma BNP has been shown to reflect the degree of ventricular dysfunction in adults with heart failure and is correlated with poor survival.[18,19] Postoperative BNP levels decrease early on after CF-LVAD implantation[20] and elevated levels even 60 days after implantation have been shown to be associated with increased mortality.[21] Serum BNP levels were elevated in both of our groups prior to placement of LVAD, albeit more elevated in patients in group 2. The exact reason for the difference is unclear but possibly suggests that these patients may be sicker than group 1. The serum BNP levels appropriately declined in both of our groups after placement of LVAD. Sato et al[21] showed that in adults, 2-year survival was significantly higher (92.0% vs 70.5%; $P = .003$) in those with 60 days serum BNP concentration <322 pg/mL as compared to those with levels ≥322 pg/mL ($P = .003$).We found a median 3 months post-LVAD BNP levels to be significantly higher in group 1 compared to group 2 (365 and 105 pg/mL) suggesting that post-operative RV dysfunction might contribute to slower myocardial recovery even in the late postoperative period.

Although the use of a RVAD has declined with the introduction of the implantable CF-VAD, along with the use of pulmonary vasodilators to lower pulmonary vascular resistance and protect RV function after LVAD implantation,[22,23] 13% of patients still require an RVAD support.[24] The operative and bypass strategies may also play a role in the postoperative RV function. All cases at our center were performed by a single surgeon with very similar perioperative management. None of the patients in our cohort needed RVAD implantation and could be supported adequately in the postoperative period. However, a significant number of patients need prolonged inotropes/pulmonary vasodilators for RV support post-CF-LVAD placement adding to the morbidity. Thus, pre-LVAD invasive hemodynamic assessment (when available) may help identify patients with higher probability of RV dysfunction. This can potentially and thereby help optimize post-LVAD medical management strategies to support the RV. This information may also be helpful to appropriately counseling families about realistic expectations post-LVAD device placement.

Although invasive hemodynamic information prior to LVAD placement when available is valuable, our findings do not propose routine invasive hemodynamic assessment in all patients prior to LVAD placement. The measurement of central venous pressures (CVP) is most commonly used to drive management decisions in perioperative period. Our data support the importance of this hemodynamic parameter in identifying patient with risk of RV dysfunction and monitoring response to therapy. Use of CVP to infer RA pressures or other RV indices can be misleading in certain clinical scenarios and should be validated before being used for advanced clinical decision making. If advanced hemodynamic assessment is performed as a part of the preimplantation evaluation (based on the discretion of the treating physician); calculation and appropriate interpretation of these hemodynamic parameters might be helpful in guiding appropriate treatment strategies. Ongoing assessment and continued surveillance of the impact of use of these hemodynamic measurements on clinical management and outcomes after CF-LVAD placement requires further investigation.

Our study has a few important limitations. The retrospective nature of our study did not allow for a planned approach to hemodynamic assessment. The decision for cardiac catheterization prior to LVAD placement was dependent on the treating physician or was a result of an additional investigation into the underlying disease. Retrospective chart review did not allow us to elucidate to the methodology behind this decision making. Due to small sample size and single institution design, only 27% of children who underwent CF-LVAD placement at our institution had preimplantation invasive hemodynamic assessment potentially limiting significance of some associations and limiting further validation.

In conclusion, invasive hemodynamic measurements as part of preoperative CF-LVAD implantation assessment have potential to provide quantitative information on RV function and may help to identify children at risk of refractory postoperative RV dysfunction evidenced by prolonged inotrope/pulmonary vasodilator requirements. Early identification of this patient population may better guide postoperative management and improve clinical outcomes.

CONFLICT OF INTEREST

None.

AUTHOR CONTRIBUTIONS

Study design: Aggarwal, Tume
Performed experiments: Aggarwal, Rodriguez
Drafted the article: Aggarwal, Tume
Critical revision of the manuscript: Adachi, Cabrera, Tunuguntla, Qureshi

REFERENCES

1. Blume ED, VanderPluym C, Lorts A, et al. Second annual Pediatric interagency registry for mechanical circulatory support (pedimacs) report: pre-implant characteristics and outcomes. *J Heart Lung Transplant*. 2018;37(1):38-45.
2. Dang N, Topkara V, Mercando M, et al. Right heart failure after left ventricular assist device implantation in patients with chronic congestive heart failure. *J Heart Lung Transplant*. 2006;25:1-6.
3. Ochiai Y, McCarthy PM, Smedira NG, et al. Predictors of severe right ventricular failure after implantable left ventricular assist device insertion: analysis of 245 patients. *Circulation*. 2002;106(12 Suppl 1):I-198-I-202.
4. Frazier OH, Rose EA, Oz MC, et al. Ventricular assist system. Multicenter clinical evaluation of the HeartMate vented electric left ventricular assist system in patients awaiting heart transplantation. *J Thorac Cardiovasc Surg*. 2001;122(6):1186-1195.
5. Kavarana MN, Pessin-Minsley MS, Urtecho J, et al. Right ventricular dysfunction and organ failure in left ventricular assist device recipients: a continuing problem. *Ann Thorac Surg*. 2002;73:745-750.
6. Fan Y, Zhang A-M, Weng Y-G, et al. Factors associated with the need of biventricular mechanical circulatory support in children with advanced heart failure. *Eur J Cardiothorac Surg*. 2013;43(5):1028-1035.

7. Deng MC, Edwards LB, Hertz MI, et al. Mechanical circulatory support device database of the International Society for Heart and Lung Transplantation: third annual report–2005. *J Heart Lung Transplant*. 2005;24(9):1182-1187.
8. Drakos SG, Janicki L, Horne BD, et al. Risk factors predictive of right ventricular failure after left ventricular assist device implantation. *Am J Cardiol*. 2010;105:1030-1035.
9. Korabathina R, Heffernan KS, Paruchuri V, et al. The pulmonary artery pulsatility index identifies severe right ventricular dysfunction in acute inferior myocardial infarction. *Catheter Cardiovasc Interv*. 2012;80(4):593-600.
10. Kang G, Ha R, Banerjee D. Pulmonary artery pulsatility index predicts right ventricular failure after left ventricular assist device implantation. *J Heart Lung Transplant*. 2016;35(1):67-73.
11. Morine KJ, Kiernan MS, Pham DT, Paruchuri V, Denofrio D, Kapur NK. Pulmonary artery pulsatility index is associated with right ventricular failure after left ventricular assist device surgery. *J Card Fail*. 2016;22(2):110-116.
12. Pediatric Registry for Mechanically Assisted Circulatory Support: Quarterly Statistical Report 2017 2nd Quarter. http://www.uab.edu/medicine/intermacs/reports/public-statistical-reports. Accessed November 17, 2017.
13. Soliman OII, Akin S, Muslem R, et al. Derivation and validation of a novel right-sided heart failure model after implantation of continuous flow left ventricular assist devices. *Circulation*. 2018;137:891-906.
14. Lopez-Sendon J, Coma-Canella I, Gamallo C. Sensitivity and specificity of hemodynamic criteria in the diagnosis of acute right ventricular infarction. *Circulation*. 1981;64(3):515-525.
15. Kormos RL, Teuteberg JJ, Pagani FD, et al. Right ventricular failure in patients with the HeartMate II continuous-flow left ventricular assist device: incidence, risk factors, and effect on outcomes. *J Thorac Cardiovasc Surg*. 2010;139(5):1316-1324.
16. Korabathina R, Heffernan KS, Paruchuri V, et al. The pulmonary artery pulsatility index identifies severe right ventricular dysfunction in acute inferior myocardial infarction. *Catheter Cardiovasc Interv*. 2012;80(4):593-600.
17. Amin A, Taghavi S, Esmaeilzadeh M, Bakhshandeh H, Naderi N, Maleki M. Pulmonary arterial elastance for estimating right ventricular afterload in systolic heart failure. *Congest Heart Fail*. 2011;17(6):288-293.
18. Yasue H, Yoshimura M, Sumida H, et al. Localization and mechanism of secretion of B-type natriuretic peptide in comparison with those of A-type natriuretic peptide in normal subjects and patients with heart failure. *Circulation*. 1994;90(1):195-203.
19. Epstein FH, Levin ER, Gardner DG, Samson WK. Mechanisms of disease: natriuretic peptides. *NEJM*. 1998;339(5):321-328.
20. Sareyyupoglu B, Boilson BA, Durham LA, et al. B-type natriuretic peptide levels and continuous-flow left ventricular assist devices. *ASAIO J*. 2010;56(6):527-531.
21. Sato T, Seguchi O, Iwashima Y, et al. Serum brain natriuretic peptide concentration 60 days after surgery as a predictor of long-term prognosis in patients implanted with a left ventricular assist device. *ASAIO J*. 2015;61(4):373-378.
22. Argenziano M, Choudhri AF, Moazami N, et al. Randomized, double-blind trial of inhaled nitric oxide in LVAD recipients with pulmonary hypertension. *Ann Thorac Surg*. 1998;65:340-345.
23. Tedford RJ, Hemnes AR, Russell SD, et al. PDE5A inhibitor treatment of persistent pulmonary hypertension after mechanical circulatory support. *Circ Heart Fail*. 2008;1:213-219.
24. Cleveland JC Jr, Naftel DC, Reece TB, et al. Survival after biventricular assist device implantation: an analysis of the interagency registry for mechanically assisted circulatory support database. *J Heart Lung Trans*. 2011;30:862-869.

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