


# Arrhythmias Following Comprehensive Stage II Surgical Palliation in Single Ventricle Patients

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**Abstract** Post-operative arrhythmias are common in pediatric patients following cardiac surgery. Following hybrid palliation in single ventricle patients, a comprehensive stage II palliation is performed. The incidence of arrhythmias in patients following comprehensive stage II palliation is unknown. The purpose of this study is to determine the incidence of arrhythmias following comprehensive stage II palliation. A single-center retrospective chart review was performed on all single ventricle patients undergoing a comprehensive stage II palliation from January 2010 to May 2014. Pre-operative, operative, and post-operative data were collected. A clinically significant arrhythmia was defined as an arrhythmia which led to cardiopulmonary resuscitation or required treatment with either pacing or antiarrhythmic medication. Statistical analysis was performed with Wilcoxon rank-sum test and Fisher's exact test with  $p < 0.05$  significant. Forty-eight single ventricle patients were reviewed (32 hypoplastic left heart syndrome, 16 other single ventricle variants). Age at surgery was  $185 \pm 56$  days. Cardiopulmonary bypass time was  $259 \pm 45$  min. Average vasoactive–inotropic score was  $5.97 \pm 7.58$ . Six patients (12.5 %) had clinically significant arrhythmias: four sinus bradycardia, one 2:1 atrioventricular block, and one slow junctional rhythm. No tachyarrhythmias were documented for this patient population. Presence of arrhythmia was associated with elevated lactate ( $p = 0.04$ ) and cardiac arrest ( $p = 0.002$ ). Following comprehensive stage II palliation, single ventricle patients are at low risk for

development of tachyarrhythmias. The most frequent arrhythmia seen in these patients was sinus bradycardia associated with respiratory compromise.

**Keywords** Arrhythmia · Hypoplastic left heart syndrome · Single ventricle · Palliation

## Introduction

Post-operative arrhythmias are common in the pediatric population following cardiac surgery and are an important cause of post-operative morbidity [10, 11, 16] and mortality [16, 17]. The incidence of post-operative arrhythmias in patients with congenital heart disease undergoing cardiac surgery has been reported to range from 14 to 48 % [1, 2, 16]. Certain factors can predispose patients to development of post-operative arrhythmias. Patient factors include lower body weight and age under 6 months [15, 17]. Operative factors include surgical technique, suture line placement, cardiopulmonary bypass time, aortic cross-clamp time, and central venous catheter location [2, 15, 21]. Certain surgical procedures for congenital heart disease have an associated risk of particular post-operative arrhythmias [2, 6], for example, ventricular arrhythmias following the Ross procedure and tetralogy of Fallot repair and junctional ectopic tachycardia (JET) status post ventricular septal defect (VSD) repair and the Fontan operation [6, 7, 10]. Finally, post-operative factors include electrolyte imbalance and exposure to inotropic agents [12, 19].

The incidence of arrhythmias in the single ventricle population has been reported following staged palliation with the Norwood, Glenn, and Fontan procedures [8, 9, 11, 14, 18, 20]. It has been described that tachyarrhythmias are common following the Norwood operation, particularly in patients who

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have received higher dose of vasoactive agents [11]. The hybrid stage I palliation, which consists of bilateral pulmonary artery band placement, a patent ductus arteriosus (PDA) stent, and balloon atrial septostomy, was developed for initial palliation of patients with hypoplastic left heart syndrome. Hybrid stage I palliation is followed by a comprehensive stage II palliation, which consists of a bidirectional Glenn, aortic arch reconstruction, and removal of pulmonary artery bands and PDA stent [4, 5, 13]. The incidence of arrhythmias in patients following comprehensive stage II palliation in the single ventricle population is unknown.

The purpose of this study is to determine the incidence of arrhythmias following comprehensive stage II palliation. The secondary aim of this study is to determine risk factors for development of arrhythmias following this procedure.

## Materials and Methods

A single-center retrospective chart review was performed on all single ventricle patients undergoing palliation with a comprehensive stage II palliation at Nationwide Children's Hospital from January 2010 to May 2014. The electronic medical record was reviewed to collect pre-operative, operative, and post-operative data.

Pre-operative data included gender, diagnosis, date of birth, admission weight, admission body surface area, diagnosis of a genetic anomaly, and echocardiographic findings (qualitative assessment of function, pulmonary band gradients, and retrograde arch gradient). Operative data collected included surgical date, cardiopulmonary bypass time, aortic cross-clamp time, circulatory arrest time, documentation of exit angiography, documentation of concerns with exit angiography and necessary intervention. Post-operative data collected included lowest documented pH, highest lactate, inotropes received (dose and duration), presence of clinically significant arrhythmias, cardiac arrest, survival, and discharge echocardiogram findings (qualitative assessment of function, pulmonary artery gradients, atrioventricular (AV) valve regurgitation). A clinically significant arrhythmia was defined as an arrhythmia which led to cardiopulmonary resuscitation (CPR), required treatment with pacing, or required treatment with an antiarrhythmic medication.

A vasoactive–inotropic score (VIS) was calculated for each patient. VIS was calculated as per Gaines et al. [3] as follows:

$$\begin{aligned} \text{VIS} = & [\text{dopamine dose } (\mu\text{g}/\text{kg}/\text{min}) + \text{dobutamine dose} \\ & (\mu\text{g}/\text{kg}/\text{min}) + 100 \times \text{epinephrine dose} \\ & (\mu\text{g}/\text{kg}/\text{min})] + [10 \times \text{milrinone dose } (\mu\text{g}/\text{kg}/\text{min}) \\ & + 10,000 \times \text{vasopressin dose } (\text{U}/\text{kg}/\text{min}) \\ & + 100 \times \text{norepinephrine dose } (\mu\text{g}/\text{kg}/\text{min})] \end{aligned}$$

The maximum VIS was calculated for 24, 48, and 72 h post-operatively. The maximum VIS for the admission was recorded, and an average VIS was calculated by averaging the maximum VIS from each of those three time periods.

Statistical analysis was performed with Wilcoxon rank-sum test for continuous data and Fisher's exact test for categorical data with  $p < 0.05$  significant. This study was reviewed and approved by the Institutional Review Board.

## Results

Forty-eight consecutive patients with single ventricle physiology undergoing comprehensive stage II palliation were reviewed. There was one patient included in all other data that was excluded from length of stay (LOS) and ventilatory data. This patient was admitted to the ICU 3 months prior to comprehensive stage II palliation for bloody stools and lactic acidosis. The patient was not discharged home prior to comprehensive stage II palliation and was chronically ventilated prior to surgery, with a goal of discharging to home on mechanical ventilation via tracheostomy. She is the only patient who underwent tracheostomy with long-term mechanical ventilation in this series of patients.

Six patients (12.5 %) had clinically significant arrhythmias. Four patients developed sinus bradycardia, one patient had 2:1 AV block, and one patient had a slow junctional escape rhythm. No tachyarrhythmias were documented for this patient population. In three of the four patients with sinus bradycardia, the clinical record described a pattern of agitation followed by hypoxia and then bradycardia. In each of these patients CPR was initiated. The fourth patient with bradycardia was first noted to develop hypotension followed by bradycardia. CPR was initiated, and the patient received temporary pacing. The clinical status of this fourth patient improved after a clot was removed from a chest tube. One patient with 2:1 AV block required DDD pacing, but had an arrest and did not survive to discharge. The patient with slow junctional rhythm required temporary AAI pacing. No patients required permanent pacemaker placement prior to discharge home.

## Pre-Operative Data

Of the patients reviewed, 32 had hypoplastic left heart syndrome (HLHS) and 16 were other single ventricle variants. There were no heterotaxy patients in this population. There was a male predominance in our population (60 %). There were no patients with a known genetic syndrome. Average weight at time of surgery was

$6.47 \pm 1.02$  kg. The average age at time of surgery was  $185 \pm 56$  days (Table 1).

## Operative Data

All patients were placed on cardiopulmonary bypass for the procedure. The median cardiopulmonary bypass time was 249 min (range 167–394 min). Twenty-five patients had aortic cross-clamp with a median time of 12 min (range 0–156 min). One patient underwent circulatory arrest with a time of 27 min. This patient had hypoplastic left heart syndrome, aortic atresia/mitral atresia variant, and had takedown of a valved main pulmonary artery to aorta conduit in addition to comprehensive stage II palliation. The presence of arrhythmias was not associated with length of cardiopulmonary bypass or aortic cross-clamp (Table 2).

## Post-Operative Data

Post-operatively, all patients at our institution are started on milrinone in the operating room with a minimum rate of  $0.25 \mu\text{g}/\text{kg}/\text{min}$ . Fifty-eight percent of patients required multiple vasoactive/inotropic infusions post-operatively (Fig. 1). There were 19 patients who received milrinone at a rate higher than  $0.25 \mu\text{g}/\text{kg}/\text{min}$ . The average VIS calculated for our patient population was  $5.97 \pm 7.58$ . The maximum VIS in this population was  $8.85 \pm 9.32$ . The presence of post-operative arrhythmia was not associated with either average or maximum VIS (Table 3).

Average hospital length of stay (LOS) was  $18 \pm 14$  days and intensive care unit (ICU) LOS  $6 \pm 5$  days. Development of arrhythmia was not associated with longer LOS. Average post-operative ventilator days were  $2 \pm 3$  days. Forty-four patients survived to discharge.

There were seven patients with a documented cardiac arrest. There was an association of having a cardiac arrest and post-operative arrhythmia ( $p = 0.002$ ). The average lowest pH was  $7.21 \pm 0.13$  ( $p = 0.564$ ). Highest post-operative lactate was  $6.11 \pm 5.95$  and was associated with post-operative arrhythmia ( $p = 0.04$ ) (Table 4).

Twenty-nine patients were on antiarrhythmic medications prior to admission for their comprehensive stage II palliation. Twenty-six patients were on digoxin alone, and three patients were on both digoxin and propranolol. It is now the standard at our institution that all patients with hypoplastic left heart are on digoxin between their Hybrid stage I and comprehensive stage II palliation. This standard was introduced during the course of this study timeline. Of the three patients on propranolol pre-operatively, two were taking the medication for a history of supraventricular tachycardia, and one was taking this medication for blood pressure control. Three patients with pre-operative medications developed a post-operative arrhythmia: One patient developed a slow junctional rhythm (pre-operatively on propranolol and digoxin), and two patients developed sinus bradycardia (pre-operatively on digoxin alone).

Following comprehensive stage II palliation, nine patients were discharged to home on antiarrhythmic medications (Table 4). Two patients were on propranolol alone, one patient was on propranolol and digoxin, and six patients were on digoxin alone at the time of discharge. Seven of these patients were on these medications prior to operation. One patient discharged home on propranolol had a documented history of supraventricular tachycardia which occurred 2 months prior to his comprehensive stage II palliation. This medication, along with digoxin, was continued at the time of discharge. There were two patients newly prescribed propranolol for blood pressure control at discharge. Neither of these patients had a documented arrhythmia. Seven patients were discharged to home on

**Table 1** Patient demographics

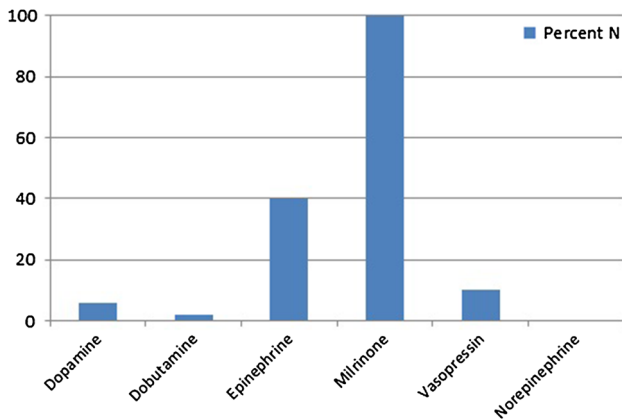
Patient demographic	Total (N)	Mean $\pm$ SD
Gender	Male = 29 Female = 19	
Diagnosis	HLHS = 32 MA/AA = 13 MS/AA = 7 MS/AS = 12 Other single ventricle variant = 16	
Genetic syndrome	Yes = 0 No = 48	
Admission weight		$6.47 \pm 1.02$ kg
Age at surgery		$185 \pm 56$ days

HLHS hypoplastic left heart syndrome, MA mitral atresia, MS mitral stenosis, AA aortic atresia, AS aortic stenosis

**Table 2** Operative data

	Overall Median (range)	No arrhythmia Median (range)	Arrhythmia Median (range)	<i>p</i> value
Cardiopulmonary bypass time ( <i>N</i> = 48)	249 min (167–394)	249 min (167–394)	283 min (204–345)	0.33
Aortic cross-clamp time ( <i>N</i> = 25)	12 min (0–156)	5 min (0–156)	36 min (0–82)	0.64
Circulatory arrest time ( <i>N</i> = 1)	0 min (0–27)	N/A	0 min (0–27)	N/A

N/A not applicable



**Fig. 1** Inotrope and vasoactive medication use following comprehensive stage II palliation

digoxin to aid right ventricular function. Two of these patients had documented sinus bradycardia. Antiarrhythmic medication use at time of discharge was not associated with presence of a post-operative arrhythmia.

**Discussion**

Our study demonstrates single ventricle patients status post comprehensive stage II palliation are at low risk for development of arrhythmias. There were no tachyarrhythmias

documented in our patients. The most frequent arrhythmia seen in these patients was sinus bradycardia associated with respiratory compromise. There were only two patients with arrhythmias reported separate from events leading to CPR. Both of these patients experienced transient arrhythmias requiring temporary pacing, and neither were discharged to home on antiarrhythmic medications.

The development of arrhythmias after surgery for congenital heart disease period is multi-factorial. We did not find any patient demographics that were associated with post-operative arrhythmias in our population. Comprehensive stage II palliation is performed at approximately 4–6 months of age, as is demonstrated by our population with an average age of 185 days. This is comparable to the timing of the Glenn operation in those patients who underwent an initial palliation with a Norwood procedure. Although there was a patient as young as 98 days, there was no association of age and development of arrhythmias.

Given the extent of the comprehensive stage II palliation and the requisite duration of cardiopulmonary bypass, we would expect that our patients would be similar to those who are status post Norwood and Glenn in terms of risk for cardiac arrhythmia. Unlike previous reports describing patients after the Norwood procedure, we did not observe any tachyarrhythmias in our patient population. There was also no association between VIS and development of

**Table 3** Post-operative data

	Overall Mean ± SD ( <i>N</i> = 48)	No arrhythmia Mean ± SD ( <i>N</i> = 42)	Arrhythmia Mean ± SD ( <i>N</i> = 6)	<i>p</i> value
Max VIS	8.85 ± 9.32	8.2 ± 8.85	11.58 ± 12.13	0.55
Average VIS	5.97 ± 7.58	5.51 ± 6.4	9.14 ± 12.7	0.55
Lowest pH	7.21 ± 0.13	7.22 ± 0.13	7.18 ± 0.12	0.56
Highest lactate	6.11 ± 5.95	5.14 ± 3.84	12.8 ± 11.2	0.04**
Ventilator days post-operatively	2 ± 3 days	3 ± 4 days	1 ± 1 days	0.56
Cardiac arrest	No = 41 Yes = 7	<i>N</i> = 3	<i>N</i> = 4	0.002**
Survival to discharge	Yes = 44 No = 4	<i>N</i> = 40	<i>N</i> = 4	0.07
ICU LOS	6 ± 5 days	7 ± 5 days	4 ± 2 days	0.16
Hospital LOS	18 ± 14 days	18 ± 15 days	16 ± 9 days	0.85

VIS vasoactive–inotropic score, LOS length of stay, ICU intensive care unit

**Table 4** Post-operative antiarrhythmic medication use

Patient	Post-operative medication	Medication administered pre-operatively	Medication indication	Post-operative arrhythmia
1	Digoxin	Yes	Support RV function	No
2	Digoxin	Yes	Support RV function	Yes—sinus bradycardia
3	Digoxin	Yes	Support RV function	Yes—sinus bradycardia
4	Digoxin	Yes	Support RV function	No
5	Digoxin	Yes	Support RV function	No
6	Digoxin	Yes	Support RV function	No
7	Digoxin	Yes	Support RV function	No
	Propranolol	Yes	Pre-operative SVT	
8	Propranolol	No	Hypertension	No
9	Propranolol	No	Hypertension	No

RV right ventricular, SVT supraventricular tachycardia

arrhythmia. Overall, our patients were on relatively lower doses of vasoactive and inotropic medications post-operatively when compared to previously reported cohorts after the Norwood procedure [11].

Studies of patients following the Glenn operation have shown patients to be at risk of both bradyarrhythmias and tachyarrhythmias [14, 20]. Much like the population examined by Reichlin et al., our patients experienced sinus bradycardia as the most frequent arrhythmia and did not require medication or pacemaker placement. They did observe tachyarrhythmias which were absent from our cohort. We documented one patient with AV block, which was not seen in their patient population [14]. Trivedi et al. describe JET as the most common post-operative arrhythmia following their stage two operation, with sinus node dysfunction also seen, but less frequently [20].

The only post-operative factors found to be associated with arrhythmia were an elevated lactate and cardiac arrest. It was inherent in our definition of clinically significant arrhythmias that cardiac arrest would be associated with arrhythmias. The association with an elevated lactate would also suggest that the more critically ill patients were likely to have arrhythmia. There was also a trend toward post-operative arrhythmia and death; however, this was not statistically significant.

There are several limitations to our study. As a single-center retrospective review, our population size is small and our data are reliant on electronic medical record documentation. There is potential for selection bias if patients had a short-lived arrhythmia that was not documented in the medical record or did not require intervention. In an attempt to capture all patients with a significant arrhythmia, we also reviewed the medication administration record to ensure capture of all patients who received an antiarrhythmic medication. We also do not have telemetry for review for each of these patients following discharge to home and thus have to assume that documented

arrhythmias were correctly identified and documented in the medical record.

In conclusion, single ventricle patients are low risk for development of arrhythmias in the immediate post-operative period following comprehensive stage II palliation. Patients with an elevated lactate or those who experience cardiac arrest are more likely to experience a post-operative arrhythmia.

#### Compliance with Ethical Standards

**Conflict of interest** The authors declare that they have no conflict of interest.

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