Title:

Norwood procedure with right ventricle to pulmonary artery conduit: A single-center 20-year experience

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Meeting presentation

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Visual abstract

Key question

What are the clinical outcomes of the Norwood procedure with right ventricle-pulmonary artery conduit for HLHC?

Key finding(s)

Fontan completion: 68.3% (93/136).

Overall survival: 80.9%, 72.3% and 62.8% at 1, 5 and 20 years, respectively.

Take-home message

Survival and Fontan completion rate was acceptable in the current staged surgical strategy with

37 RV-PA Norwood procedure.

Abstract (word count = 241)

Objectives: The aim of this study was to evaluate the long-term outcomes of the Norwood procedure with right ventricle-pulmonary artery (RV-PA) conduit for hypoplastic left heart complex (HLHC).

Methods: A retrospective observational study was performed in 136 patients with HLHC who underwent a Norwood procedure with RV-PA conduit between 1998 and 2017. The probabilities of survival, reintervention and Fontan completion were analyzed.

Results: Stage 1 survival was 91.9% (125/136). Reintervention for pulmonary artery stenosis was needed for 22% and 30% at stage 2 and 3, respectively, while 15% underwent reintervention for aortic arch recoarctation. Among 106 bidirectional Glenn survivors, 93 (68% of the total number of patients) had a Fontan completion, while four were not considered to be Fontan candidates. Risk factors for overall mortality included weighing <2.5 kg at the time of the Norwood procedure, intact atrium septum, total anomalous pulmonary vein connection, and more than mild atrioventricular regurgitation at the time of the Norwood procedure. Overall survival was 80.9%, 72.3% and 62.8% at 1, 5, and 20 years, respectively.

Conclusions: Probabilities of survival and Fontan completion were acceptable under the current surgical strategy incorporating RV-PA Norwood procedure as the first palliation. Incorporating a strategy to maintain pulmonary artery growth and ventricular function through the staged repair is of prime importance. Further studies are necessary to observe changes in atrioventricular regurgitation as well as in right ventricular function, in patients who require atrioventricular valve interventions during the staged Fontan completion.

Keywords

Hypoplastic left heart complex, Norwood, RV-PA conduit, Fontan completion, Tricuspid regurgitation

ABBREVIATIONS AND ACRONYMS

AVVR, atrioventricular valve regurgitation

BDG, bidirectional Glenn

Bil.PAB, bilateral pulmonary artery banding

BTS, Blalock-Taussig shunt

HLHC, hypoplastic left heart complex

HLHS, hypoplastic left heart syndrome

IAS, intact atrium septum

PA, pulmonary artery

PAI, pulmonary artery index

PS, pulmonary artery stenosis

RVEDP, right ventricular end-diastolic pressure

RVEF, right ventricle ejection fraction

RV-PA, right ventricle-pulmonary artery

TAPVC, total anomalous pulmonary vein connection

TCPC, total cavopulmonary connection

TR, tricuspid regurgitation

TVP, tricuspid valve plasty

INTRODUCTION

Hypoplastic left heart syndrome (HLHS) is characterized by undeveloped left-sided heart structures that are insufficient to sustain systemic circulation (1). Norwood stage palliation greatly improved the outcomes of patients with HLHS; however, performing the Norwood procedure with a modified Blalock-Taussig shunt (BTS) is technically challenging and still carries significant mortality and morbidity (2). Despite successful reconstructive surgery, death often occurs in the first 24 to 48 hours after surgery due to hemodynamic instability secondary to the unpredictable rapid fall in pulmonary vascular resistance (3).

The introduction of right ventricle-pulmonary artery (RV-PA) conduit as an alternative to modified BTS resulted in an unprecedented excellent early survival after the Norwood procedure. The resultant high diastolic pressure (i.e., high coronary artery pressure), lower aortic saturation, and a decreased volume work improved myocardial perfusion and ventricular function (4,5). Computational modeling analyses have shown that hemodynamic performance after Norwood procedure with an RV-PA conduit is more effective than after the procedure with a modified BTS (6).

We have previously reported early survival results after Norwood stage 1 palliation (7). In this study, we sought to see both short and long-term results, including probabilities of survival and reintervention after the Norwood procedure, as well as completion of the Fontan operation at our institution.

MATERIALS AND METHODS

A single-center retrospective observational study was performed using the medical records of 136 patients with HLHS or HLHS variants who underwent a modified Norwood procedure using the RV-PA conduit at Okayama University Hospital between January 1998 and December 2017. This retrospective observational study was approved by the institutional review board on March 31, 2019, and the requirement to obtain informed consent was waived. High-risk patients for the primary Norwood procedure met the following criteria: 1) gestational age, <37 weeks, 2) body weight, <2.5 kg at birth, 3) more than moderate atrioventricular valve regurgitation (AVVR), 4) organ failure, or 5) cerebral hemorrhage. Some, but not all of these patients received bilateral pulmonary artery banding (Bil.PAB) prior to the Norwood procedure. Six patients subsequently underwent Norwood and bidirectional Glenn (BDG) procedures and all survived. These six patients were excluded as no RV-PA conduit was used.

The medical and operative records, and angiographic and echocardiographic data for all patients were reviewed. Anatomic diagnosis was based on a review of echocardiography and operative findings. Follow-up status was determined by reviewing medical records and through contacts with the referring cardiologists.

Surgical technique

Details on the operative procedures used in this study have been reported previously (5,7). Briefly, the following technical modifications for the RV-PA conduit were performed: for patients weighing up to 3.5 kg, a 5-mm expanded polytetrafluoroethylene (ePTFE) ringed conduit was used. Autologous pericardium was initially used in 10 patients to patch the distal main PA;

however, this was changed to cuffed ePTFE tubes due to early obstruction of the main PA. Initially, a right ventriculotomy at the outlet portion was made using a knife; however, this was changed to a coronary puncher to create a consistent small hole.

Statistical analysis

Continuous variables were reported as the median (interquartile range) for skewed data, or the mean (standard deviation) for normally distributed values, while categorical variables were reported as absolute frequency (percentage). Continuous variables were compared using Student's *t* -test or Mann-Whitney U test, based on the normality of the data. Categorical variables were compared using Fisher's exact test or chi-square test. Survival was assessed using Kaplan-Meier analysis, and differences between groups were analyzed using the log-rank test. Competing risk outcomes were analyzed with a cumulative incidence function. Exclusive endpoints were death, Fontan completion, and the remaining patients being alive without Fontan completion. As a result, we used a non-parametric method to estimate the cumulative incidence function from a specific cause over time using the %CIF macro in SAS.

Risk factors for time-related outcomes were tested using Cox regression analysis. Univariate analysis identified variables with a *P* value <0.10, and these were then entered into a multivariate Cox proportional hazards regression model in a stepwise fashion to determine the independent predictors of outcomes. Hazard ratios (HRs) and 95% confidence intervals (CIs) were reported for significant multivariate risk factors. The level of statistical significance was set at *P* <0.05. All statistical analyses were performed with SPSS version 22 (Chicago, IL) or SAS version 9.3 (Cary,

NC).

RESULTS

Patients' characteristics

Patients' characteristics are shown in Table 1. A total of 109 patients had classical HLHS, and the remaining 27 had variants of HLHS with left ventricular and aortic arch hypoplasia, consisting of the following diagnoses: double-outlet right ventricle with systemic outlet obstruction (n = 8), ventricular septal defect with critical aortic stenosis, coarctation of the aorta, or interrupted aortic arch (n = 16) and heterotaxy syndrome (n = 3). Intact atrium septum (IAS) was associated with six patients (4%). During the study period, 30 patients with high-risk status received Bil.PAB as the first palliation.

Median age at the time of Norwood procedure was nine (range: 4–25) days, and median weight was 3.0 (range: 2.6–3.2) kg. Twenty-six patients (18%) weighed less than 2.5 kg. Ten patients (7%) were premature (gestational age <37 weeks). More than mild AVVR was associated with 27 patients (20%), and RV dysfunction (defined as less than 50% of RV ejection fraction [RVEF]) was associated with four patients (3%). Mean lower body arrest, mean myocardial ischemic, and mean cardiopulmonary bypass time were 55 ± 18 minutes, 57 ± 20 minutes, and 148 ± 36 minutes, respectively.

Operative mortality of Norwood procedure

Stage 1 survival was 91.9%. Operative mortality, defined as death within 30 days if discharged or

no time limit if remaining in the hospital, occurred in 11 patients (8%). Causes of death included sudden death (n = 3), heart failure (n = 3), desaturation due to pulmonary hypertension (n = 2), septic shock (n = 2), and tamponade (n = 1). Body weight <2.5 kg, mitral atresia/aortic stenosis, IAS, total anomalous pulmonary vein connection (TAPVC), and RV dysfunction affected operative mortality, while preceding Bil.PAB did not affect operative mortality (*P* = 0.71) (Table 1).

Follow-up

Clinical outcomes for all patients are summarized in Figure 1. Mean follow-up duration was 109 ± 78 months. There were eight late deaths after the Norwood procedure. These occurred due to desaturation caused by shunt obstruction (n = 4), sudden death (n = 2), suffocation caused by milk aspiration (n = 1), or respiratory syncytial viral bronchiolitis (n = 1). Among stage 1 survivors (n = 117), four patients received an additional systemic-pulmonary artery shunt followed by biventricular repair. The BDG procedure was performed in 110 patients. Four patients died in the hospital from heart failure (n = 1), heparin-induced thrombocytopenia (n = 1), BDG obstruction (n = 1), or mediastinitis (n = 1). There were nine late deaths after BDG procedure due to heart failure (n = 5), septic shock (n = 2), or pneumonia (n = 1). One patient required take-down of BDG circulation due to central venous high pressure and eventually died from heart failure. Four patients could not achieve Fontan completion; reasons for this failure are listed in Table 3. Therefore, 87 patients underwent a total cavopulmonary connection (TCPC) procedure. One patient died in the hospital due to intracranial bleeding. Eleven late deaths occurred after the TCPC procedure due to heart failure (n = 7), rupture of the esophageal varices (n = 2), thrombosis of the conduit (n = 1), or arrhythmia (n = 1).

Reintervention

Surgical intervention for recoarctation of the neo-aortic arch was required in 17 patients (15%) at stage 2, and 5 patients (6%) at stage 3. Atrioventricular valve plasty was performed in 17 patients (15%) at stage 2, and 21 patients (24%) at stage 3, including valve replacement with a mechanical valve (n = 1). Catheter intervention for recoarctation of the neo-aortic arch was required in 19 patients (17%) at stage 2, and 7 patients (8%) at stage 3.

PA growth and ventricular function

Cardiac catheterization was performed before the BDG (n = 117) and TCPC (n = 103) procedures (Table 2). After BDG, the RVEF decreased significantly from 66 (range: 60–73) to 57 (range: 52–63) percent, P <0.001; however, right ventricular end-diastolic pressure (RVEDP) did not change significantly. Before the BDG procedure, 26 (22%) patients developed pulmonary artery stenosis (PS), while 33 (30%) patients developed PS before the TCPC procedure. The PA index did not differ between stage 2 and stage 3 (208 [range: 163–261] vs. 215 [range: 173–253] mm^2/m^2, P = 0.58).

Failing to achieve Fontan completion

Among 106 stage 2 survivors, four patients failed to achieve Fontan completion. The patients' courses are summarized in Table 3. All patients had both RV dysfunction and severe hypoplastic

PA. Patient 1 had preserved RV function with trivial AVVR; however, she suffered severe left PS after stage 1, and her PA did not grow despite a left PA plasty. Furthermore, an advanced atrioventricular block caused dyssynchrony of the RV, which deteriorated the RV function. Patient 2 had moderate AVVR before the BDG procedure and underwent tricuspid valve plasty (TVP) at the time of the BDG procedure. However, the remaining moderate AVVR caused a low ejection fraction (EF) and high RVEDP, eventually causing poor pulmonary artery index (PAI) values. Patient 3 had cerebral palsy after stage 1 due to hemodynamic instability, which required emergency resuscitation. He also underwent TVP at stage 2, but moderate AVVR remained. Furthermore, he suffered severe left PA stenosis, causing hypoplastic PA. Patient 4 not only had moderate AVVR before stage 2, but also had pulmonary high flow status. Before stage 3, her RV function deteriorated, followed by poor PAI values due to high RVEDP.

Risk analysis of overall mortality and long-term outcomes

Multivariate analysis indicated that risk factors for overall mortality included body weight <2.5 kg at the time of the Norwood procedure (HR 3.02; 95% CI: 1.49–6.15, *P* <0.001), IAS (HR 6.70; 95% CI: 2.63–17.1, *P* <0.001), TAPVC (HR 4.88; 95% CI: 1.44–16.6, *P* = 0.011), and more than mild AVVR (HR 2.85; 95% CI: 1.51–5.38, *P* <0.001) (Table 4). Overall survival was 80.9%, 72.3%, and 62.8%, and the probability of Fontan completion was 6.6%, 45.6%, and 64.0% at 1, 5, and 20 years, respectively (Figure 2A).

Survival was stratified by the presence or absence of AVVR at the time of Norwood procedure. Survival was higher in patients with equal or less than trivial AVVR than in those with more than

mild AVVR. Overall survival in equal or less than trivial AVVR patients was 88.9%, 76.2%, and 70.3% at 1, 5 and 20 years, respectively, vs 55.6%, 32.0%, and 32.0% in patients with more than mild AVVR (P <0.001; Figure 2B).

DISCUSSION

In our 20-year experience with using the RV-PA conduit in Norwood stage 1 palliation, stage 1 survival was 92%, which was the same as the survival reported 10 years ago (7). These positive results are due to the introduction of RV-PA conduit, various surgical techniques and thoughtful perioperative care. Although questions about the appropriate systemic-pulmonary shunt and risk factors for Norwood stage 1 mortality have been debated, long-term experience at a single-institution have rarely been reported.

We analyzed the factors affecting operative mortality at stage 1 and variations in PA conditions and ventricular function to understand long-term problems, particularly the failure to achieve Fontan completion, and overall mortality. In our study, low weight at the time of surgery, IAS, TAPVC, and RV dysfunction were found to be risk factors at stage 1. Despite often requiring a reintervention for PS, adequate PA growth was obtained in most of the patients. Patients who did not achieve Fontan completion had reduced PA index and RV dysfunction. More than mild AVVR at the time of the Norwood procedure gradually exacerbated RV function as a systemic chamber, leading to long-term mortality.

Operative mortality of Norwood procedure

As many studies have reported (7-9), low weight at surgery, IAS, TAPVC, and RV dysfunction are risk factors affecting operative mortality after the Norwood procedure. Our strategy for high-risk patients is to perform a Bil.PAB procedure prior to the Norwood procedure to observe pulmonary function. Since preceding Bil.PAB did not affect operative mortality, our strategy to perform rapid two-stage (i.e., Bil.PAB following Norwood procedure in approximately one month) appears to be reasonable for patients with a low body weight and gestational age.

PA growth and ventricular function

The size of the PA is an important factor for an optimal passive pulmonary perfusion in Fontan circulation (10). In fact, four patients in our study were not able to achieve Fontan completion due to having a small PA. The absence of a pulmonary pumping chamber for active blood supply to the lungs in HLHS patients results in a low-pulsatile flow into the pulmonary arteries and underfilling of the pulmonary vascular bed (11). Therefore, 20% of our patients at each stage underwent PA plasty for morphologic PS which led to high pulmonary artery pressure and a small PA. Because of the “parallel” circulation with a systemic-pulmonary shunt, the preload for the RV is large compared to the “in-series” circulation after a BDG procedure, which reflects hyperkinetic RV before BDG. Therefore, BDG should be performed around six months of age to preserve ventricular function.

Anatomic and physiologic uniqueness of HLHS

In our institution, management of HLHS patients has had a goal of restricting the pulmonary blood

flow to preserve ventricular function, while partially clipping the RV-PA conduit at the time of cessation of cardiopulmonary bypass or a delayed sternal closure. Reduced pulmonary blood flow/systemic blood flow (Qp/Qs) was also able to preserve tricuspid valve function. Although Qp/Qs was not evaluated in this study, the fact that RVEDP in HLHS patients did not differ reflected the difference of Qp management. RV function in HLHS patients might deteriorate not only from regurgitation of the tricuspid valve caused by high Qp/Qs as the atrioventricular valve of the systemic chamber, but also by a recoarctation of the aortic arch. A propensity score-matched, multi-institutional large cohort study was performed by the Congenital Heart Surgeons' Society (12), in which the authors found that late RV dysfunction and late tricuspid regurgitation (TR) were not different between an RV-PA group and a BTS group.

Another concern for HLHS patients is PA growth. In this study, PA plasty as a concomitant procedure was required frequency. In addition to the management of low Qp/Qs, a high incidence of morphologic PS might be related to low PAI. In most cases, a retracted main PA by RV-PA conduit was confirmed by computed tomography, according to the body growth and RV. PA hypoplasia and stenosis are well-recognized complications after the Norwood procedure (13). Honjo *et al.* reported that a preventive patch plasty of the branch PA was performed in the vast majority of the patients at stage 2, as it is widely accepted that PA growth is not obtained after BDG (14, 15).

Overall mortality and its risk factors

Unlike other factors as IAS, TAPVC, RV dysfunction, and low weight at the time of the Norwood

procedure, more than mild AVVR at the time of the Norwood procedure was identified as a sole risk factor for overall mortality. Figure 2B shows the stepwise decline of overall survival even after the Fontan completion in patients with more than mild AVVR. Most of these patients died of heart failure. This finding indicates that a failing RV in systemic circulation that is gradually exacerbated by AVVR is not compatible with lifelong health. Some may suggest that heart transplantation is the best choice for these patients; however, this is not a realistic management option in our country. Alsoufi *et al.* described that annular dilatation was an important component of TR in all patients, and a fair number of those patients (14/30) had associated structural anomalies (16). An association with structural anomalies is expected to continue to have a significant regurgitation despite repetitive TVP (16, 17). Subsequently, residual TR continues to deteriorate RV function, which is reported as one of the two determinants of late outcomes following the Fontan procedure, and is related to longevity of TV competence (12, 17, 18).

LIMITATION

The current report had the typical limitations of a retrospective observational study. Specifically, changes in perioperative management during the study period may have affected our results. In addition, the rarity of this disease meant we had a small cohort size, and the multiple variables described in this study were a consequence of different surgical approaches.

CONCLUSION

Application of the RV-PA conduit yielded early excellent results, as well as high probability of

achieving Fontan completion and long-term survival. Incorporating a strategy to maintain these factors through staged repair is important. TR had a negative impact on overall survival. Therefore, future studies to measure changes in TR as well as in RV function are necessary in those requiring intervention on TV during the staged Fontan completion.

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Funding and Conflict of interest: None to declare

FIGURE LEGENDS

Figure 1. The current status of all hypoplastic left heart syndrome or variant patients.

Figure 2. (A) Competing risk analysis of clinical outcomes, (B) Kaplan-Meier analysis for overall survival stratified by atrioventricular valve regurgitation

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327 **TABLES**

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Table 1. Demographics (n = 136) and Factors Associated with Operative Mortality of Norwood Procedure							
Characteristics	Overall (n = 136)		Survivors(n = 125)		Mortality (n = 11)		*P* value
Male gender	76	(56)	69	(55)	7	(64)	0.59
Age at NW (days)	9	(4–25)	7	(4–26)	12	(6–24)	0.90
Weight at NW (kg)	3.0	(2.6–3.2)	3.0	(2.6–3.3)	2.5	(2.2–3.0)	0.023
Weight at NW <2.5 kg	26	(18)	20	(16)	6	(54)	0.002
Premature birth	10	(7)	8	(6)	2	(18)	0.15
Genetic or extracardiac anomalies	16	(12)	15	(12)	1	(9)	0.77
HLHS subtype							
MA/AA	54	(40)	53	(42)	1	(9)	0.030
MA/AS	7	(5)	4	(3)	3	(27)	0.001

MS/AA	30	(22)	26	(21)	4	(36)	0.23
MS/AS	18	(13)	17	(14)	1	(9)	0.67
HLHS variants	27	(20)	25	(20)	2	(18)	0.88
Classical HLHS	109	(80)	100	(80)	9	(81)	0.88
Associated anomaly							
Intact atrium septum	6	(4)	4	(3)	2	(18)	0.020
TAPVC	4	(3)	2	(2)	2	(18)	0.002
Right ventricular dysfunction	4	(3)	2	(2)	2	(18)	0.002
Atrioventricular regurgitation >- mild	27	(20)	23	(18)	4	(36)	0.16
Ascending aorta diameter < 2.0 mm	12	(9)	9	(7)	3	(27)	0.024
preceding Bil.PAB	30	(22)	27	(22)	3	(27)	0.71
CPB time (min)	148	±36	144	±33	180	±55	0.072
Myocardial ischemia time (min)	57	±20	57	±20	60	±21	0.64
Lower body arrest time (min)	55	±18	55	±17	56	±24	0.77
Data presented as median (interquartile range) or n (%) or mean (±SD). NW, Norwood;							

HLHS, hypoplastic left heart syndrome; AA, aortic atresia; AS, aortic stenosis; MA, mitral atresia; MS, mitral stenosis; TAPVC, total anomalous pulmonary vein connection; Bil.PAB, bilateral pulmonary artery banding; CPB, cardiopulmonary bypass.

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Table 2. Evaluation of PA Growth and Cardiac Function in HLHS Patients

Variables	before BDG (n = 117)		before TCPC (n = 103)		*P* value
Catheterization					
RVEF (%)	66	(60–72)	57	(52–63)	<0.001
RVEDP (mmHg)	7	(6–7)	6	(5–7)	0.92
PA index (mm^2/m^2)	208	(163–262)	215	(173–253)	0.58
Right PA pressure (mmHg)	12	(11–14)	11	(9–13)	<0.001
Left PA pressure (mmHg)	13	(12–15)	11	(9–13)	<0.001
PA resistance (W/U)	1.7	(1.2–2.0)	1.6	(0.9–2.0)	0.55
Morphologic PS	26	(22)	33	(30)	0.101

Data presented as median (interquartile range) or n (%). PA, pulmonary artery; HLHS, hypoplastic left heart syndrome; BDG, bidirectional Glenn; TCPC, total cavopulmonary connection; RVEF, right ventricular ejection fraction; RVEDP, right ventricular end-diastolic pressure; PS, pulmonary artery stenosis.

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Table 3. Summary for patients who are not Fontan candidates

Patient	subtype	preceding Bil.PAB	Weight at NW (kg)	Age at NW (days)	AVVR at NW	previous AVVP	latest AVVR
1	MA/AA	yes	2.9	61	trivial	no	mild
2	MA/AA	yes	3.2	62	mild	yes	moderate
3	MS/AA	yes	2.8	121	trivial	yes	moderate
4	MS/AA	no	3.2	7	mild	yes	moderate

Bil.PAB, bilateral pulmonary artery banding; NW, norwood; AVVR, atrioventricular valve regurgitation; AVVP, atrioventricular valvuloplasty; EF, ejection fraction; EDP, end-diastolic pressure; PAP, pulmonary artery pressure; PAI, pulmonary artery index; Qp/Qs, pulmonary blood flow/systemic blood flow ratio; PS, pulmonary artery stenosis; AA, aortic atresia; AS, aortic stenosis; MA, mitral atresia; MS, mitral stenosis; BDG, bidirectional Glenn; PA, pulmonary artery; RV, right ventricle; TVP, tricuspid valve plasty

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Latest catheter examination						
EF (%)	**EDP (mmHg)**	**PAP (mmHg)**	**PAI (mm^2/m^2)**	**Qp/Qs**	**PS**	**Reason of Fontan not achieved**
43	10	16	113	0.55	yes	RV dysfunction + hypoplastic PA
56	11	12	95	0.87	no	RV dysfunction + hypoplastic PA
54	12	15	105	0.74	yes	RV dysfunction + hypoplastic PA
58	11	17	157	0.56	no	RV dysfunction + hypoplastic PA

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Table 4. Univariate and Multivariate Analysis of Risk factors For Overall Mortality (n = 136)						
Characteristics	Survivors (n = 92)		Mortality (n = 44)		*P* value (Univariate)	HR (95% CI); *P* value (Multivariate)
Male gender	50	(54)	26	(59)	0.60	
Age at NW (days)	8	(4–36)	9	(4–18)	0.47	
Weight at NW (kg)	3.0	(2.7–3.3)	2.7	(2.3–3.1)	0.008	
Weight at NW <2.5 kg	9	(10)	17	(38)	<0.001	3.02 (1.49–6.15); *P* = 0.002*
Premature birth	3	(3)	7	(15)	0.008	1.20 (0.41–3.53); *P* = 0.74
Genetic or extracardiac anomalies	13	(14)	3	(6)	0.22	
HLHS subtype						

MA/AA	41	(45)	13	(29)	0.094	0.60 (0.30–1.20); *P* = 0.14
MA/AS	3	(3)	4	(9)	0.15	
MS/AA	18	(20)	12	(27)	0.31	
MS/AS	12	(13)	6	(13)	0.92	
HLHS variants	18	(20)	9	(20)	0.90	
Associated anomaly						
Intact atrium septum	0	(0)	6	(100)	<0.001	6.70 (2.63–17.1); *P* <0.001*
TAPVC	1	(1)	3	(6)	0.06	4.88 (1.44–16.6); *P* = 0.011*
Right ventricular dysfunction	0	(0)	4	(9)	0.003	3.09 (0.70–13.0); *P* = 0.13
Atrioventricular regurgitation >- mild	11	(12)	16	(36)	0.001	2.85 (1.51–5.38); *P* <0.001*
Ascending aorta diameter <2.0 mm	6	(7)	6	(13)	0.13	
preceding Bil.PAB	25	(27)	6	(13)	0.078	0.72 (0.28–1.86); *P* = 0.50

Data presented as median (interquartile range) or n (%). HR, hazard ratio; CI, confidence interval; NW, Norwood; HLHS, hypoplastic left heart syndrome; AA, aortic atresia; AS, aortic stenosis; MA, mitral atresia; MS, mitral stenosis; TAPVC, total anomalous pulmonary vein return; Bil.PAB, bilateral pulmonary artery banding

Only variables having a *P* value <0.10 in the univariable analysis are entered into the multivariable Cox regression model

* *P* value <0.05 (multivariate)

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Figure1

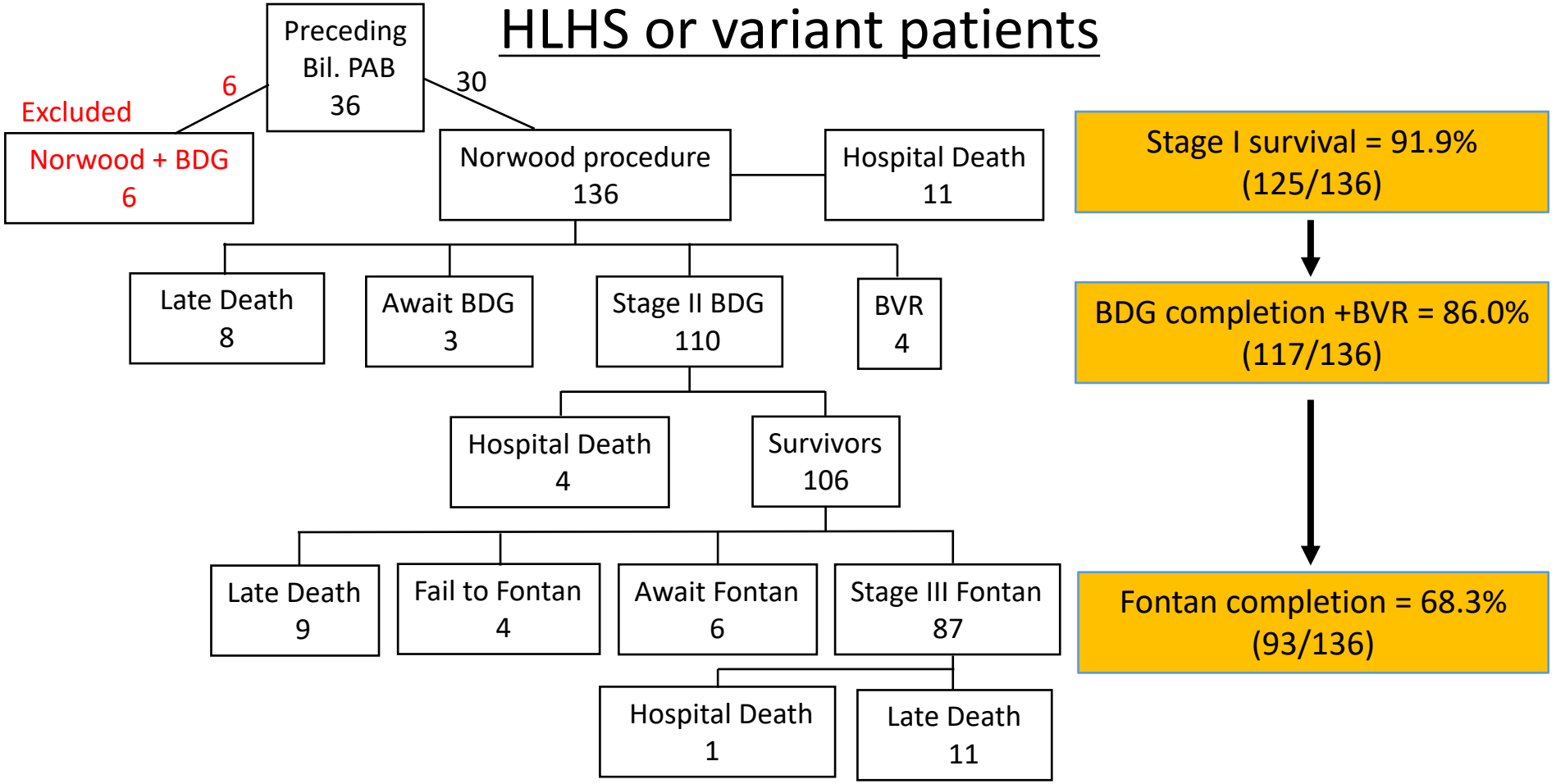

HLHS or variant patients
Preceding
Bil. PAB
36
6
Excluded
Norwood + BDG
6
30
Norwood procedure
136
Hospital Death
11
Late Death
8
Await BDG
3
Stage II BDG
110
BVR
4
Hospital Death
4
Survivors
106
Late Death
9
Fail to Fontan
4
Await Fontan
6
Stage III Fontan
87
Hospital Death
1
Late Death
11
Stage I survival = 91.9%
(125/136)
BDG completion +BVR = 86.0%
(117/136)
Fontan completion = 68.3%
(93/136)

Figure2A

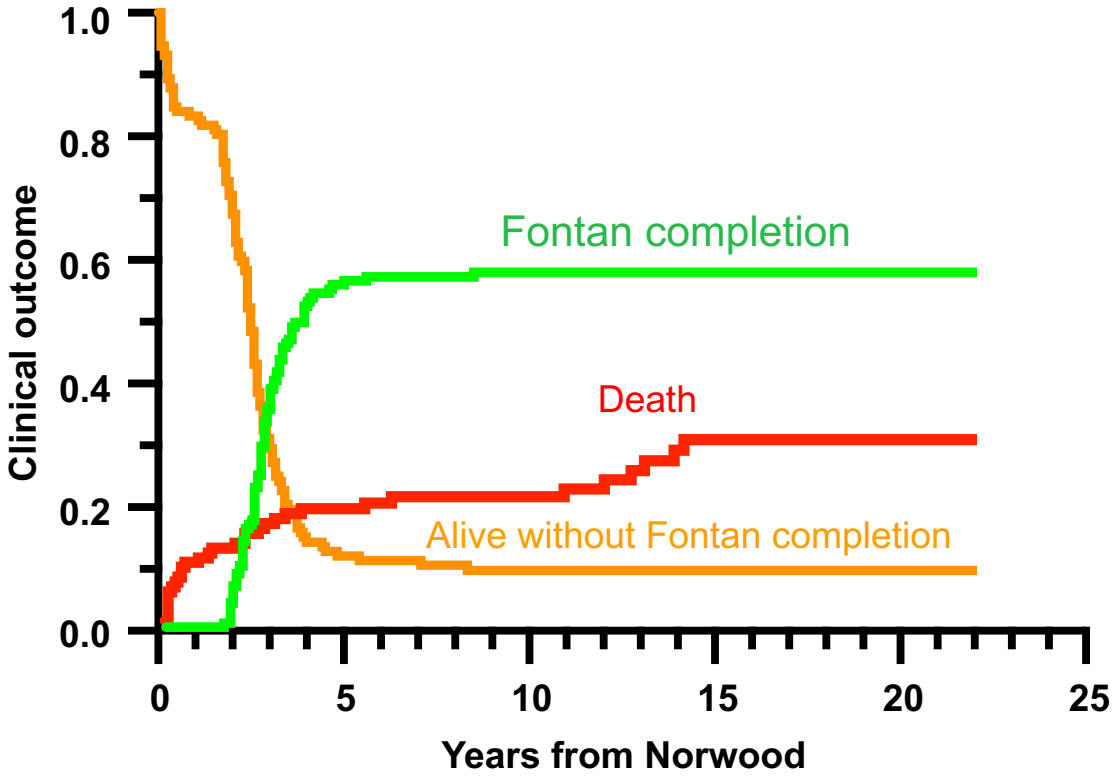
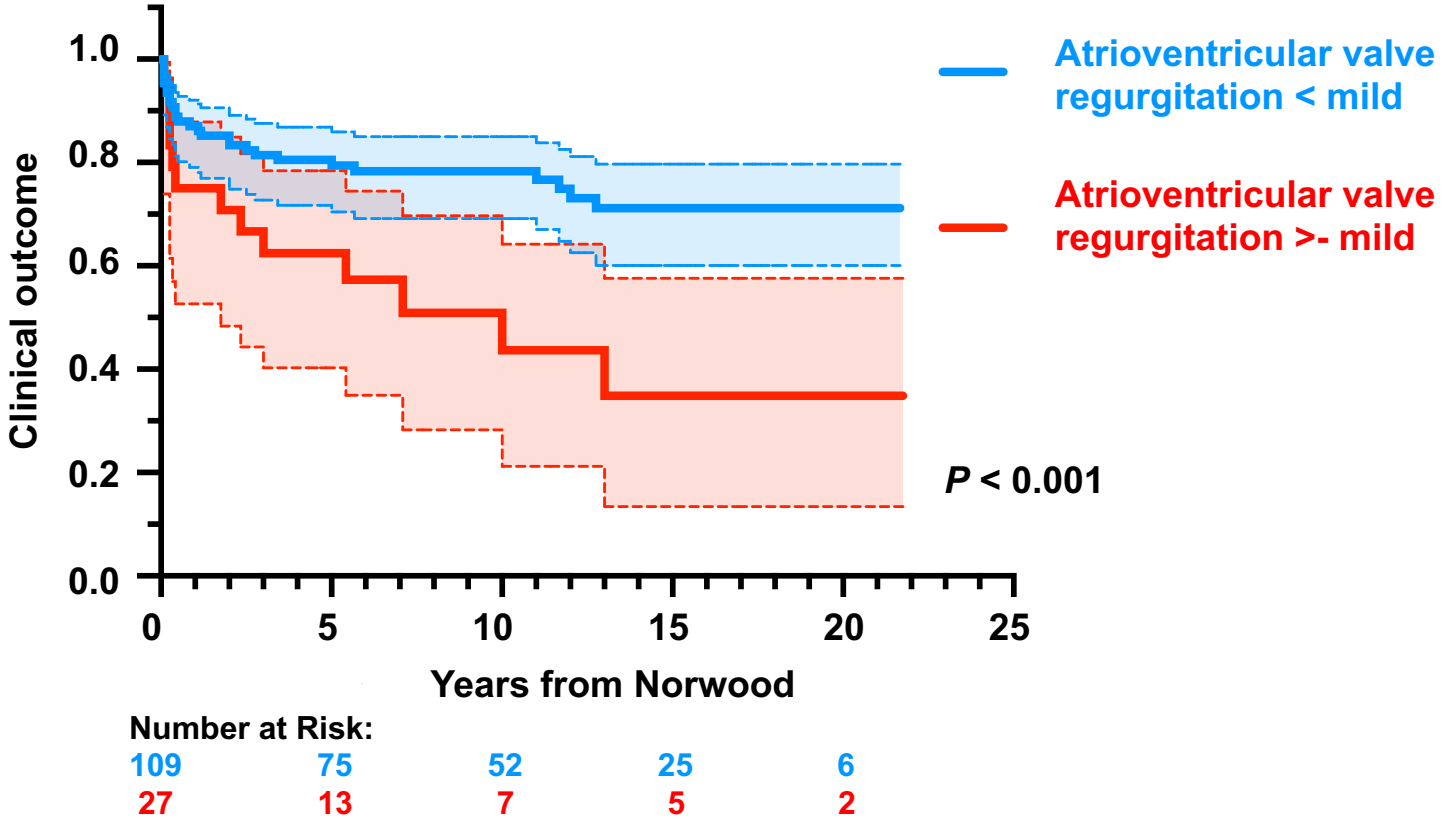

1.0
0.8
0.6
0.4
0.2
0.0
Clinical outcome
Fontan completion
Death
Alive without Fontan completion
0
5
10
15
20
25
Years from Norwood

Figure2B


Clinical outcome
1.0
0.8
0.6
0.4
0.2
0.0
0
5
10
15
20
25
Years from Norwood
Atrioventricular valve regurgitation < mild
Atrioventricular valve regurgitation >- mild
P < 0.001
Number at Risk:
109 75 52 25 6
27 13 7 5 2