Hybrid Approach for Hypoplastic Left Heart Syndrome: Intermediate Results After the Learning Curve

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Background. **Lessons learned during the development of a novel hybrid approach have resulted in a reliable, reproducible alternative treatment for hypoplastic left heart syndrome (HLHS). Herein we report our results using this hybrid approach in a uniform risk cohort.**

Methods. **This is a review of prospectively collected data on patients treated for HLHS using a hybrid approach (n = 40) between July 2002 and June 2007. The hybrid approach includes pulmonary artery bands, a ductal stent, and atrial septostomy as a neonate, comprehensive stage 2 procedure resulting in Glenn shunt physiology at six months and Fontan completion at two years.**

Results. **Forty patients had a hybrid stage 1 with 36 undergoing a comprehensive stage 2 procedure. Fifteen patients have completed the Fontan procedure with 17 pending. Overall survival was 82.5% (33 of 40). The seven deaths included one at stage 1, two between stages 1 and 2, three at stage 2, and one between stages 2 and 3. One patient had successful heart transplantation during the interstage period.**

Conclusions. **The hybrid approach can yield acceptable intermediate results that are comparable with a traditional Norwood strategy. Potential advantages of the hybrid approach include the avoidance of circulatory arrest and shifting the major surgical stage to later in life. These data provide the platform for a prospective trial comparing these two surgical options to assess whether there is less cumulative impact with the hybrid approach, thereby improving end organ function, quality, and quantity of life.**

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The hybrid approach for the management of hypoplastic left heart syndrome (HLHS) has been developed as an alternative strategy that involves a less invasive initial procedure; combining surgical techniques (branch pulmonary artery banding) and interventional cardiology techniques (stenting of the ductus arteriosus and balloon atrial septostomy), thereby shifting the risk of the major open heart surgery to an older age. Our previous report on this approach focused on the lessons learned during the development of this technique [1, 2]. Now, with a reliable, reproducible technique we report our intermediate results with emphasis on the combined risks of the hybrid stage 1 + 2 as well as the interstage period. To help assess the intrinsic value of this hybrid approach, only patients without known high risk characteristics are included.

Patients and Methods

Patient Population

Sixty-two patients underwent a hybrid stage 1 procedure between July 2002 and June 2007. To have a uniform risk cohort that reflects a typical patient with HLHS we excluded patients with non-HLHS univentricular anatomy, those bridged to a two ventricle repair, patients at known high risk including intact atrial septum, weight less than 1.5 kg, significant extracardiac malformations such as congenital diaphragmatic hernia, and those previously reported as part of the learning curve. The remaining 40 patients all have typical HLHS (aortic atresia or critical stenosis with mitral atresia or stenosis). A review of prospectively collected data including information from all planned staged procedures, any unplanned reinterventions, and interstage outcomes are discussed herein. Follow up was complete in all patients. Patient characteristics are listed in Table 1. This study was approved by the Institutional Review Board (0503HS090), given the retrospective nature and absence of any patient identification, requirement for individual patient consent was waived.

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Table 1. Hybrid Patient Characteristics

	Diagnosis	Age 1 (days)	Weight 1 (kg)	Stage 2	Age 2 (days)	Weight 2 (kg)	Stage 3	Current Status	Stage of Death
1	AA/MA	12	2.1	Yes	151	4.9	Yes	Alive	
2	AA/MA	5	3.2	Yes	94	4.1	Yes	Alive	
3	AA/MA	6	3.4	Yes	76	5.7	Yes	Alive	
4	AS/MS	5	2.8	Yes	91	5.7	Yes	Alive	
5	AA/MA	9	3.8	Yes	91	5.2	Yes	Alive	
6	AA/MS	14	3.4	Yes	132	5.1	Yes	Alive	
7	AA/MA	7	3	Yes	122	4.8	Yes	Alive	
8	AS/MS	10	3.6	Yes	109	6	No	Dead	2
9	AS/MS	3	2.6	Yes	205	5.9	No	Dead	2
10	AA/MA	5	3.1	Yes	237	5	Yes	Alive	
11	AA/MA	7	3.6	Yes	182	5.5	Yes	Alive	
12	AA/MA	6	3.5	Yes	213	6.3	Yes	Alive	
13	AA/MA	4	3.9	Yes	184	7.7	Pending	Alive	
14	AS/MA	5	3.3	Yes	161	6.4	Yes	Alive	
15	AS/MS	9	2.5	No			No	Dead	Interstage 1-2
16	AA/MA	7	4.4	Yes	221	7	Yes	Alive	
17	AS/MS	11	2.2	Yes	189	5.4	Yes	Alive	
18	AA/MA	13	2.2	Yes	199	4.1	Pending	Alive	
19	AS/MS	10	3.4	Yes	216	6.3	No	Dead	Interstage 2-3
20	AA/MA	15	3.5	Yes	225	5.3	Yes	Alive	
21	AA/MA	8	3.1	Yes	217	7	Yes	Alive	
22	AA/MA	7	3	Yes	193	5.9	Pending	Alive	
23	AS/MS	14	2.6	No			No	Dead	1
24	AA/MS	11	2.3	Yes	234	5.3	Pending	Alive	
25	AA/MA	16	3.65	Yes	240	7.4	Pending	Alive	
26	AA/MA	7	2.3	Yes	145	5.7	Pending	Alive	
27	AA/MA	5	3.4	Yes	145	5.7	Pending	Alive	
28	AS/MA	10	3.3	Yes	131	5.6	Pending	Alive	
29	AS/MS	2	3.1	Yes	161	6.6	No	Dead	2
30	AA/MA	5	2.3	No			No	Dead	Interstage 1-2
31	AA/MA	6	2.9	Yes	139	5	Pending	Alive	
32	AA/MA	4	3.7	Yes	205	7	Pending	Alive	
33	AS/MS	4	3.1	Yes	189	7.1	Pending	Alive	
34	AA/MS	2	3.2	No			No	Alive	
35	AA/MS	8	3.5	Yes	188	5.8	Pending	Alive	
36	AA/MA	4	3.6	Yes	155	5.3	Pending	Alive	
37	AA/MA	4	3.3	Yes	178	6.5	Pending	Alive	
38	AS/MS	9	1.5	Yes	180	5.2	Pending	Alive	
39	AA/MA	7	3.2	Yes	177	4.1	Pending	Alive	
40	AA/MS	14	3.3	Yes	175	5.9	Pending	Alive	
Median		7	3.2		180	5.7			
Mean		7.7	3.1		172	5.8			

AA = aortic atresia; AS = aortic stenosis; MA = mitral atresia; MS = mitral stenosis.

Methods

CONTRAINDICATION TO A HYBRID STAGE 1. Anatomic variations that are not considered a contraindication include aortic atresia, a diminutive ascending aorta, patient weight, malposed great arteries, dextrocardia, situs inversus, or heterotaxy syndrome. However, one lesson learned [1] is to recognize an unusual anatomic variant of HLHS with congenital stenosis of the retrograde orifice to the transverse aortic arch, which can become immediately compromised when a ductal stent is deployed. Typically, children with HLHS, even those with aortic atresia, have an adequate-sized transverse aortic arch that opens even further at the connection with the ductus arteriosus. This area of connection can be effectively imaged and assessed preoperatively by echocardiography (Fig 1). If there are signs of flow acceleration consistent with a stenotic retrograde orifice, these patients are not considered candidates for a hybrid stage 1. They can undergo a modified hybrid stage 1 that assures flow into the transverse aorta either by placement of an additional stent

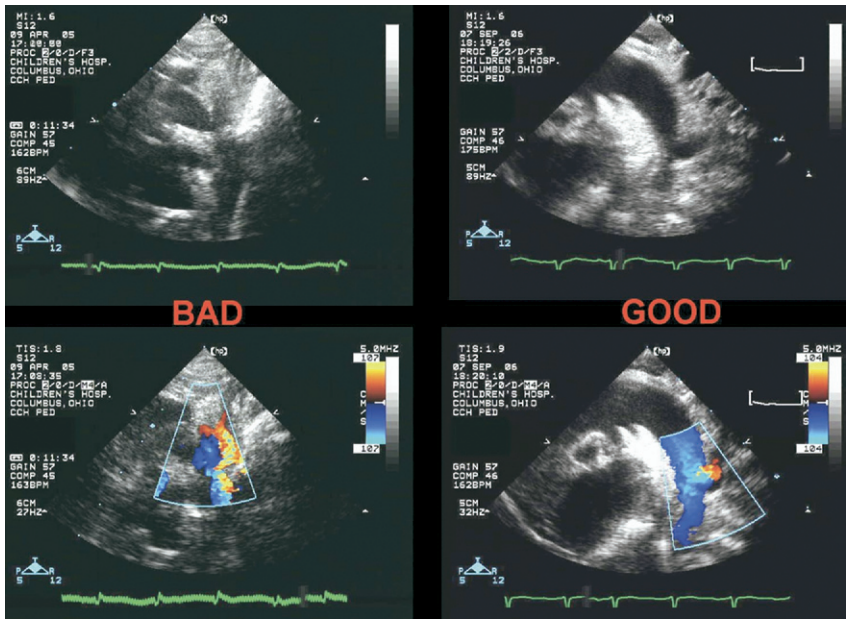

Fig 1. This series of echocardiograms focus on the origin of the retrograde orifice of the transverse aortic arch where it connects to the ductus arteriosus. The right-side panels show unobstructed retrograde flow into the transverse aortic arch. The left-side panels show this area with and without color flow mapping illustrating a stenotic retrograde orifice and hence a contraindication to a hybrid stage 1 procedure.

across this stenotic area, reported by the group in Geissen, Germany [3, 4] or by creation of a reverse central shunt, reported by the group in Toronto, Canada [5]. Our preference is to refer these patients for a traditional Norwood procedure.

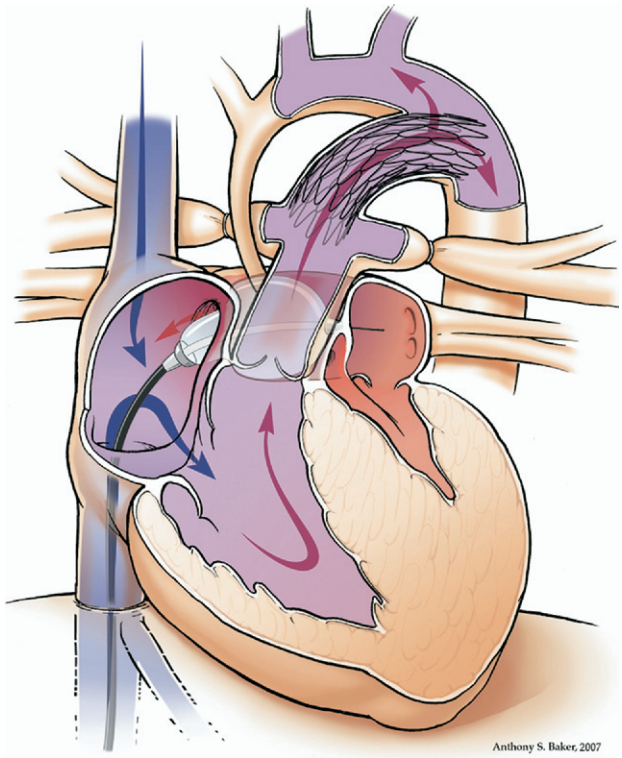

Fig 2. The hybrid stage 1 palliation. Branch pulmonary artery bands and a stent across the patent ductus arteriosus are placed at one procedure, while the balloon atrial septostomy is performed as a separate procedure.

HYBRID STAGE 1. The goals of the hybrid stage 1 palliation include the following: (1) unobstructed systemic output through the patent ductus arteriosus (PDA); (2) improved balance of the pulmonary and systemic circulations; and (3) an unobstructed atrial septal defect (Fig 2). Technical details of the hybrid stage 1 procedure have been previously reported by our group [1, 2]. Under general anesthesia, by a median sternotomy, off cardiopulmonary bypass bilateral branch pulmonary artery (PA) bands are placed. The bands are fashioned by cutting a 1- to 2-mm ring from a 3.5-mm Gortex tube graft (W. L. Gore & Associates, Inc, Flagstaff, AZ) and passing them around the branch PA. A 3.0-mm graft is used for patients weighing less than 2.5 kg. The left PA band is placed immediately after its takeoff from the main PA. The right band is positioned between the ascending aorta and the superior vena cava. Once positioned the bands are tacked to the local adventitia. The degree of band tightening is judged based on patient size, caliber of the branch PA, response in systemic blood pressure and oxygen saturation to tightening, as well as angiographic appearance of the bands. Typically, there is a 10-point increase in systolic blood pressure and a 10-point decrease in oxygen saturation. Banding first is important to optimize the hemodynamics by balancing the pulmonary and systemic circulations. Next, through a sheath in the main PA, using angiographic control, an appropriate sized stent is placed. The important point is to completely cover the PDA, which typically extends from the left PA past the retrograde orifice of the transverse aorta. Treatment of the atrial septum by balloon atrial septostomy is performed as a separate procedure just prior to the patient going home or when the mean Doppler gradient by echocardiography is 8 or more. This delay allows the interventional cardiologist to perform a more durable septostomy by using a bigger balloon (2 mL) in a larger left atrium.

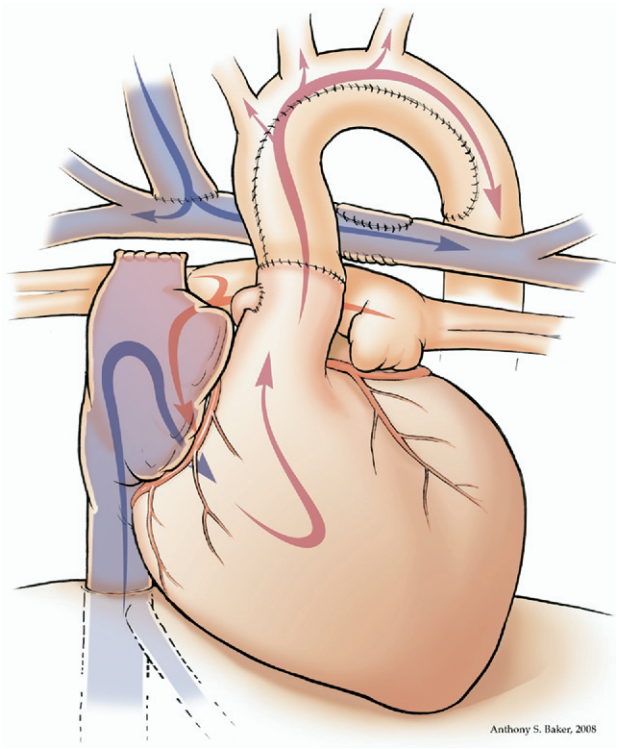

Fig 3. The comprehensive stage 2. This illustration demonstrates the resultant anatomy after a comprehensive stage 2 procedure.

INTERSTAGE MONITORING. After discharge, the infants are followed closely with every one- to two-week cardiology assessment. Echocardiography is used liberally to monitor for obstruction at the atrial septum or through the PDA stent, either antegrade down the descending aorta or retrograde into the transverse aortic arch. Decreased right ventricular function or increased tricuspid regurgitation is seen as an early indication of obstruction. Any evidence of obstruction or decreased ventricular function leads to a catheterization to diagnose and treat the level of obstruction. We no longer routinely perform a surveillance or precomprehensive stage 2 catheterization. The patients are scheduled for comprehensive stage 2 surgery at four to six months of age.

COMPREHENSIVE STAGE 2. The open heart surgery consists of removal of the PDA stent and PA bands, repair of the aortic arch and pulmonary arteries (if necessary), division of the diminutive ascending aorta with reimplantation into the pulmonary root, main PA to reconstructed aorta anastomosis, atrial septectomy, and a bidirectional cavopulmonary anastomosis (Fig 3). Procedures were performed on cardiopulmonary bypass with aortic cross-clamping. Circulatory arrest is not needed because of the transverse arch growth, which allows it to be directly cannulated with advancement of the cannula into the innominate artery during arch reconstruction. The PDA stent was completely removed and the aortic arch reconstructed with a patch of pulmonary homograft in all patients. The right PA was only augmented by positioning the cavopulmonary anastomosis across the area of the previous band. Left PA patch augmentation was judged necessary in nearly half the patients.

Table 2. Hybrid Stage 1 Results

Time to extubation	52% in OR 85% in 24 hours
Inotrope score	0 (0–12)
Time to enteral feed	79% in 24 hours
Postoperative ICU (days)	4.5 (1–26)
Postoperative LOS (days)	13 (4–32)
Patient charges	$92,270
Hospital survival	97.5%

ICU = intensive care unit; LOS = length of stay; OR = operating room; Data = median (range).

Table 3. Comprehensive Stage 2 Results

Time to extubation	47% in OR 86% in 24 hours
Inotrope score	0 (0–3)
Lactate level mmol/L	2.3 POD 0 1.1 POD1
Time to enteral feed	81% in 24 hours
Postoperative ICU (days)	4 (2–31)
Postoperative LOS (days)	7.5 (4–35)
Patient charges	$80,204
Hospital survival	92%

ICU = intensive care unit; LOS = length of stay; OR = operating room; POD = postoperative day; Data = median (range).

Results

Hybrid Stage 1

A hybrid stage 1 was performed on 40 patients with HLHS (70% aortic atresia) at a median age 7 days and weight 3.2 kg. Postoperative outcomes are shown in Table 2. Only seven patients received blood products. Fifty-two percent were extubated in the operating room while 85% were extubated within 24 hours. The median inotrope score [6] was 0, only two patients had a score 3 or greater. The median time to first enteral feed was postoperative day (POD) 1 with 79% taking enteral feeds within 24 hours. Length of stay in the intensive care unit (ICU) was a median of 4.5 days (mean, 6.7) while the hospital stay was a median of 13 (mean, 14.2). No patient required a delayed sternal closure or extracorporeal membrane oxygenation (ECMO) support. There was 97.5% hospital survival (39 of 40). The one death was a patient who had an uncomplicated procedure, progressing appropriately toward discharge. On POD15 the patient aspirated, suffering a respiratory arrest, and expired despite resuscitative measures. Hospital charges were a median of $92,270 (mean, $111,990).

Interstage 1 - 2

There were two interstage deaths; 5% (2 of 39) mortality. Both patients had infectious etiologies with probable dehydration prior to sudden cardiopulmonary arrest at home, four and six weeks postoperatively. One of them

Table 4. Combined Stage 1+2 Results

	Hybrid Approach (Stage 1+2)
Bypass (min)	291 (159–459)
Cross-clamp (min)	85 (26–158)
DHCA (min)	0 (0–46)
Hours ventilated	9 (0–141)
Postoperative ICU (days)	8 (3–31)
Postoperative LOS (days)	21 (10–64)
Blood usage (ml/kg)	88 (0–195)
Patient charges	$179,759

DHCA = deep hypothermic circulatory arrest; ICU = intensive care unit; kg = kilogram; LOS = length of stay; min = minutes; mL = milliliters; Data = median (range).

had additional risk factors; weight 2.3 kg, Turner syndrome, and Dandy-Walker malformation.

One patient underwent successful heart transplantation six months after the hybrid stage 1 for ventricular failure. Six weeks after an uncomplicated hybrid stage 1 the patient required stenting of a restrictive atrial septum. This was complicated by heart block requiring a pacemaker. Over the ensuing months his ventricular function deteriorated without any evidence of obstruction, flow limitation, or imbalance in the circulation.

There were two reoperations. One to replace a left PA band that opened after the stitch broke one month postoperatively. The second reoperation was to recover an embolized atrial septal stent deployed to treat a restricted atrial septum five weeks after the hybrid stage 1. Both patients went on to a successful comprehensive stage 2.

There were 12 reinterventions in the catheterization laboratory in ten patients; all successfully relieved the level of obstruction and all patients went on to a comprehensive stage 2. Two interventions were aimed at the atrial septum (one balloon + one stent), seven interventions were aimed at antegrade flow through the PDA (two angioplasty + five stent), and four stents were placed to relieve retrograde stenosis into the transverse aortic arch. Feeding gastrostomy tubes were required in six patients.

Prior to the comprehensive stage 2, the echocardiographic assessment of right ventricular function was graded as normal in all but two patients in whom it was graded as mildly depressed. Tricuspid regurgitation was trivial in all but three patients, mild in two, and only one with moderate tricuspid regurgitation, which required valvuloplasty at the comprehensive stage 2.

Comprehensive Stage 2

A comprehensive stage 2 procedure was performed in 36 patients at a median age of 180 days and 5.7 kg weight. Median bypass and cross-clamp times were 291 and 85 minutes, respectively. Only the first two patients had a period of circulatory arrest. Milrinone (0.25 mcg/kg/min) was started routinely on all patients. The postoperative echocardiographic assessment of right ventricular function was graded as normal in 80% with only one patient having greater than mild dysfunction or greater than mild tricuspid regurgitation. Postoperative data are listed in Table 3. Eighty-six percent (31 of 36) of patients were extubated within the first 24 hours. Median inotrope score the first day was 0. Median lactate level was 2.3 mmol/L on arrival to the ICU, and 1.1 mmol/L on POD 1. Eighty-one percent of patients returned to enteral feeds within 24 hours. The median length of stay in the ICU was four days (mean, 5.4) and hospital stay was median 7.5 (mean, 9.5). One patient had a subdural hematoma that required no intervention, while no patient had a seizure. No patient required dialysis and the urinary output was greater than 1 cc/kg/hour during the first 24 hours in all patients. No patient required a delayed sternal closure or ECMO support. All patients were in normal sinus rhythm except one patient who had transient accelerated junctional rhythm.

There were three deaths; 8% (3 of 36) mortality. The first patient died POD 5 of refractory ventricular arrhythmias. Autopsy revealed a transmural infarction of the small, hypertrophied left ventricle (aortic stenosis-mitral stenosis) with unobstructed coronary arteries. The second death occurred POD 3, in a previously hemodynamically stable, intubated patient, of unclear etiology. Review of the records did not demonstrate an arrhythmia, electrolyte imbalance, or other clear cause and an autopsy was not granted. The final death on POD 26 was in a patient who, just prior to discharge home, developed a fulminate pneumonia leading to empyema, sepsis, and multisystem organ failure. The hospital charges were a median of $80,204 (mean, $100,708).

Interstage 2 - 3

One patient died six months postoperatively of a nosocomial infection, multisystem organ failure after being readmitted with a chylothorax. Five patients required placement of a left PA stent. No patient required reintervention at the aortic arch.

Fontan Completion

Fifteen patients underwent a successful Fontan completion with no mortality, while 17 are awaiting Fontan completion. One patient had a tricuspid valve repair at the time of surgery, while no patient required further pulmonary artery augmentation.

Hybrid Stage 1 + Comprehensive Stage 2

Table 4 combines postoperative variables for the hybrid stage 1 plus comprehensive stage 2 procedures. The parameters of cardiopulmonary bypass have continued to shorten with experience; median bypass and cross-clamp times were 291 and 85 minutes, respectively. Two patients received no blood products through both hybrid stage 1 and 2 procedures, nor at the Fontan completion. Overall utilization of all blood products was a median of 88 mL/kg (mean, 87 mL/kg) with no patient requiring reoperation for bleeding. Total hours on the ventilator were median 9 (mean, 31). Total combined number of days in the ICU were median 8 (mean, 10.8) and in-

hospital were median 21 (mean, 24.4). Total hospital charges were a median $179,759 (mean, $205,428).

Comment

The results of the staged surgical palliation for HLHS have improved significantly over the years. Nonetheless, the overall morbidity and mortality of the initial Norwood procedure and its impact on the long-term success of the resulting Fontan circulation remain suboptimal [7]. Recent enthusiasm for the use of a right ventricle (RV)-PA conduit instead of a modified Blalock-Taussig (BT) shunt during the Norwood procedure has not significantly changed the overall survival [8–10]. Important information about these two options will be forthcoming from the National Heart, Lung, and Blood Institute sponsored multicenter prospective, randomized clinical trial that is currently underway.

An alternative to the traditional Norwood approach is the hybrid approach for the management of HLHS. The primary goal of the approach is to create a stable, balanced circulation without the use of open heart surgery (bypass, cross-clamp, circulatory arrest) with its associated risks in a neonate. The major open heart surgical procedure is thereby shifted to later in life at an age when a circulation in series can be established with a cavopulmonary anastomosis. Early reports on the initial outcomes of the hybrid approach [1, 3, 4] were limited by the impact of the learning curve of this new therapy, small cohorts of patients with mixed diagnoses and risk stratification, as well as short follow-up. Subsequent reports have focused on the use of the hybrid approach in high risk HLHS patients [11–13]. Importantly, to truly assess the risks of the hybrid approach as compared with the Norwood approach, both stage 1 and 2 results as well as the interstage period need to be considered.

The goal of our report is to evaluate the benefits and risks of the hybrid approach in a uniform cohort of patients with HLHS, including stage 1 and 2, so that a reasonable comparison can be made to patients treated with the Norwood approach. This is the largest single institution experience with this hybrid approach, which is offered to all patients with HLHS. The only exclusion criterion is echocardiographic evidence of restricted flow into the retrograde transverse aorta from the ductus arteriosus. This was noted in three patients who went on to a successful traditional Norwood procedure. Although Norwood, hybrid, and transplant surgical options are offered to all families, there were no primary transplants performed and only eight Norwood procedures reflecting an institutional bias for the hybrid approach.

In this report patients with weights greater than 1.5 kg were included, even though 2.5 kg is commonly used as the cutoff for high risk. We consider weight less than 1.5 kg to be higher risk, but not the range between 1.5 kg and 2.5 kg for the hybrid approach.

Our results of the hybrid stage 1 procedure indicate a low impact, low risk procedure, where 80% are extubated and on enteral feeds within 24 hours, blood usage and inotropic support are rare, delayed sternal closure or ECMO are not necessary, the ICU stay is short, and hospital survival is 97.5%.

Interstage mortality (5%) and reintervention rate (36%) are similar to those reported for the Norwood procedure. Our reintervention rate may be high because we utilize close interstage monitoring with echocardiography and take an aggressive approach to maintaining unrestricted flow through the PDA stent, both antegrade and retrograde, as well as maintaining an unrestricted atrial septal opening.

Our treatment of the atrial septum has evolved. The key is not allowing the atrial septum to become restrictive because this is associated with significant thickening of the atrial septum making subsequent interventions more complicated and less effective. This was evident in two patients with serious complications (embolization and heart block) related to atrial septal stenting. Now we perform a balloon atrial septostomy before the child is discharged but separate this procedure from the PA banding-PDA stent component of the hybrid stage 1. This simple delay allows some enlargement of the left atrium in a more stable patient, which enables the interventional cardiologist to perform a more aggressive balloon (2 mL) atrial septostomy resulting in a significant enlargement and durable tear of the septal tissue. We have not needed to reintervene at the atrial septum on any patient treated with this technique.

Only 10% (4 of 40) of patients developed significant retrograde stenosis into the transverse aorta. All were effectively treated by placing an additional retrograde stent and went on to a successful comprehensive stage 2. Given this low incidence we do not recommend a prophylactic reverse central shunt [5]. Moreover, given our experience in three patients with this type of shunt, the unknown physiology it creates with the potential of a coronary steal, and the more complicated postoperative course in patients with this shunt reported in the literature [14], we no longer use a reverse central shunt.

Although the comprehensive stage 2 procedure is a long operation involving essentially all the steps of a traditional Norwood stage 1+2 procedure, plus removal of the PDA stent and PA bands, the results show that the postoperative course is more similar to that of a Norwood stage 2 only. Our results indicate that the majority (85%) are extubated within 24 hours, inotropic support greater than the empiric use of milrinone is rare, right ventricular function is preserved, and indicators of overall perfusion are normal by lactate, renal function, lack of seizures, and no ECMO requirements. This picture is presumably because the patients have a low risk profile (normal ventricular function, no end organ dysfunction, protected pulmonary bed) going into the operation. Then the conduct of the operation minimizes end organ ischemia with the majority of the procedure performed on bypass with a beating heart and no circulatory arrest time, while the resultant circulation in series with a cavopulmonary shunt is more stable than a circulation in parallel such as the case with a Norwood stage 1.

Two published series from the Children's Hospital Boston [8, 9] and the Children's Hospital of Philadelphia

Table 5. Comparative Data from Published Series

	NCH-Hybrid Approach n = 40	CHB-BTS n = 46	CHB-RVPA n = 34	CHOP-BTS n = 95	CHOP-RVPA n = 54
Mortality stage 1	2%	11%	15%	14%	17%
Mortality interstage	5%	14%	0%	17%	5%
Interstage reintervention	36%	33%	27%	18%	37%
Rate of weight gain (gm/day)	16 (9–33)	16.5 (10–60)	20.6 (10–40)		
Gastrostomy tube	6 pts	6 pts	1 pt		
Moderate or severe RV dysfunction pre-2	0%	4%	10%		
Moderate or severe TV regurgitation pre-2	3%	26%	16%		
Moderate or severe RV dysfunction post-2	3%				
Moderate or severe TV regurgitation post-2	3%				
Mortality stage 2	8%				
Open sternum 1 or 2	0%	92%	79%	23%	33%
ECMO 1 or 2	0%	19%	7%	14%	13%
Combined hospital LOS, 1+2	21	33	22	18	18.5
Overall survival (“usual risk”)	82.5%	76%	79%	68% (“86%”)	74% (“86%”)

BTS = Blalock-Taussig shunt; CHB = Children’s Hospital Boston; CHOP = Children’s Hospital of Philadelphia; Data = median (range); ECMO = extracorporeal membrane oxygenation; LOS = length of stay in days; NCH = Nationwide Children’s Hospital; pt = patient; RV = right ventricle; RVPA = right ventricle to pulmonary artery conduit; TV = tricuspid valve.

[10] include information on patients with HLHS through Norwood stage 1+2. The focus of these contemporary reports is to compare outcomes of patients initially treated with a BT shunt versus a RV-PA conduit. Both institutions conclude that the overall outcomes are not different between shunt types. Please note that these reports include both standard and high risk patients with HLHS. Table 5 lists outcome variables for the hybrid approach with similar information, where available, from these published series [8–10] for the Norwood approach. Overall survival for the hybrid approach was 82.5% (33 of 40). One series [10] had an overall survival of 86% among a subgroup of patients with a “usual risk” profile that was comparable with the cohort in our report. Interstage mortality was low for the hybrid approach, similar to rates reported for the RV-PA shunt patients but lower than that for the BT shunt patients. The need for interstage reintervention was similar across all groups. Some potential indicators of morbidity in terms of the need for delayed sternal closure, ECMO support, or right ventricular dysfunction were less with the hybrid approach. Nonetheless the overall combined time spent in the hospital was similar across all groups. Long-term follow up will be necessary to see if these differences impact the outcomes after the Fontan completion in terms of end organ function, quality of life, and longevity. We will continue to follow our patients to specifically evaluate neurologic, cardiac, and psychosocial measures of outcome.

Another interesting area of research will be what impact does moving the biologic stressors of major open heart surgery from the neonatal period to a later stage of infancy by comparing inflammatory mediators at the cellular and organ level in HLHS patients undergoing a Norwood stage 1 versus a comprehensive stage 2 procedure. By shifting the age of the bypass, there may be a dramatic impact to the patient’s neurologic development. In this prospective review, we had one patient with a neurologic event, a subdural hematoma, which resolved spontaneously, while no patient had any seizures. After completing all three stages, patients with HLHS have significant neurocognitive difficulties [15]. Part of the neurocognitive deficiency is related to the fact that patients with HLHS have structural abnormalities in the brain [16]. However, neonates who undergo complex congenital heart surgery have a 34% increase in periventricular leukomalacia, a nonspecific sign of cerebral white matter injury, postoperatively [17]. Most likely, neonates with HLHS have a fragile central nervous system and the initial surgical repair, which includes placing them on cardiopulmonary bypass with the necessary deep hypothermic arrest, can lead to neurological injury [18]. Use of the hybrid stage 1 procedure has the benefit of delaying the necessity of bypass until the brain is more developed. This delay may have the benefit of better long-term neurologic outcomes.

While the patient data were collected prospectively, this review is a descriptive assessment, limited by a small, nonrandomized patient population and an institutional bias, for the hybrid approach. In conclusion, our study supports the use of the hybrid approach for the management of HLHS patients with the usual risk profile.

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DISCUSSION

DR ROBERT D. B. JAQUISS (Little Rock, AR): That was a spectacular series, just amazing, stunning even. I think everybody would agree that an hour's worth of cardiopulmonary bypass support when you're a week old and prone to inflammatory mediators, and all the other evils that go along with bypass, is quite different than having an hour's worth of support when you're six months old. I wanted to ask you about the organ that's most at risk, the brain. You alluded to the importance of long-term follow-ups, but you've got enough kids out now far enough that maybe you could do some neurodevelopmental analyses, such as PIDI or MIDI or other acronymic confusions that address how these kids are developing and whether they've got spatial and psychomotor abnormalities.

Do you have any data along those lines yet because I think that's really where the money is going to be. If people can do what Jim Tweddell was talking about with the conventional approach and do what you're talking about with the hybrid approach, we can probably expect survival in the 80% to 85% range at a year with usual-risk patients. I think those data are pretty clear.

But if one group has to take Ritalin or Adderall or similar medications and is a real bear to take care of, and the other group are doing fine and are nice little kids, I think I know which way I'd go.

DR GALANTOWICZ: I appreciate your comments, and you're absolutely right that it will be important to see whether these midterm differences carry forth.

One of the concerns with the hybrid approach is with the stage I. The cerebral blood flow is dependent on that retrograde orifice, which is not as large as the orifice will be after a Norwood stage I arch augmentation. And although there's no clinical evidence of neurologic impact at this point, there may be important subclinical neurologic impact.

And so we now almost have enough patients that are three years or more out to appropriately look at that. At this point we can make no comment or have no important information to share about that.

DR MARSHALL L. JACOBS (Philadelphia, PA): These are spectacular results, and the lessons from this presentation are immense.

I think for a lot of institutions the learning curve associated with the Norwood procedure, both from a technical operative standpoint and an ICU management standpoint, was perhaps substantial in a variable length from one place to another. You were very, very candid in your introduction about the difference between this experience you report today and the earlier experience that you reported previously.

With respect to this entire experience, what fraction of it is accounted for as your period of learning curve and what fraction is the later period where you think you've ironed out most of the kinks? And, of course, one hopes that in your manuscript the lessons of the learning curve period will all be articulated so that people won't have to reproduce them.

My compliments. But how long was the learning curve period compared to this period of stunning results?

DR GALANTOWICZ: I appreciate your comments, Dr Jacobs. The nine patients were considered part of the learning curve and were excluded from this series. We did publish a paper that talks about the lessons learned that specifically try to limit the learning curve for others embarking on this approach.

Our goal, really, here today was to try and give a picture of the usual hypoplast patient with a standard risk profile to help

everybody that's looking at this approach whether or not it is reasonable to use in their institution given their own results. And many places are using the hybrid approach for high risk patients, and it's harder to decipher the value or the potential benefits or risk of the approach.

So this was a uniform patient population of true hypoplast with a very standard risk profile.

DR JAMES S. TWEDDELL (Milwaukee, WI): I thought it was an excellent study, excellent outcomes, and I think you are really on to something. I applaud your innovation and your willingness to take the road less traveled.

This is highly dependent on technology. Could you speculate on what new technological innovations might help bring the hybrid approach to its fullest potential? Two areas in particular in which technological innovations might be helpful include the management of proximal arch obstruction that is observed in some patients. Could that be stented? What about ASD [atrial septal defect] creation, is there a way to more reliably create an ASD noninvasively? Thank you. I really appreciate it. Nice study.

DR GALANTOWICZ: Those are excellent questions. Sort of moving backwards, the ASD was initially the Achilles heel for us with this procedure, and most of the reinterventions were at the atrial septal defect.

With the simple modification of delaying addressing the atrial septum to just prior to discharge, which is about a week later, there's some growth in the left atrium, there's stabilization of the child, and it allows the interventional cardiologist to use a larger or really a standard Rashkind balloon and get a very formidable tear such that at the comprehensive stage II procedure there's really no atrial septum to take out. So once we adopted that technique, there's only been one reintervention at the atrial septum.

I think the retrograde flow into the arch, we have started at this point to not prospectively treat the retrograde flow by stenting it open and only treating it if it shows evidence of stenosis, and then you can put a stent through the PDA [patent ductus arteriosus] stent into the retrograde orifice and stent it open.

Whether that can be addressed initially, and certainly the group in Toronto have tried to address that by doing a sort of reverse BT [Blalock-Taussig] shunt, if you will, from the main PA [pulmonary artery] to the arch, I think that will be an important question. Whether the amount of blood flow that's getting through there is adequate, we don't have the answer to that until we have further neurologic follow-up.

In terms of what your team would need and the technological demands of this, they're really not out of the realm of what all of our groups are doing. Banding is a very straightforward technique surgically. The stenting of the PDA in this context, where the sheath is placed in the main pulmonary artery for an interventional cardiologist, is really within their usual armamentarium.

I think the spirit of collaboration and the close follow-up and the need to reintervene frequently is probably the most important aspect of a successful hybrid approach.

DR PETROS V. ANAGNOSTOPOULOS (Phoenix, AZ): Would you please comment a little bit about the technical aspects of this second operation? Especially touch on the technical difficulties of taking the stent out from the duct.

DR GALANTOWICZ: Your question and Jim's tie together. The hardest part of this whole procedure, I and II combined, is taking the stent out of the aortic arch. As the child grows in that intervening six months, the aorta or the stent moves downstream and posteriorly in the patient, and it's harder to get to that area in a six-month old than it is in a six-day old. And as we all know, if you get a tear there, your treatment options are limited and certainly significant.

So we have designed the conduct of the operation so that period of taking the stent out of the aortic arch is not under circulatory arrest. You can take your time, and it's essentially an endarterectomy, if you will, or a peeling out of the stent. But you're left with half of the media and only adventitia, so it is a thin area. And then it's augmented in the usual way that a Norwood arch augmentation is done.

You have to believe that in the future there will be absorbable stents. When that day comes, this will be very easy because you'll just fillet open the arch and use your patch augmentation, and that main hurdle will be taken away.

So part of our group's hope is that as technology advances, the soundness of this approach will only improve with improved technology.

DR CHRISTOPHER A. CALDARONE (Toronto, Ontario, Canada): Mark, when you resect the stent, invariably there's some tissue left behind that has been stented open. And looking at it, it's difficult to tell whether it's duct that's been stented open and stuck in that position or if it's aorta; very difficult to tell.

Do you always resect all tissue that's been underneath the stent, or do you leave some tissue behind which may or may not include some old ductal tissue?

DR GALANTOWICZ: No, we do not resect all tissue that's been covered by the stent because we purposely stent past the transverse arch past what you would think anatomically is the ductus into the descending thoracic aorta. So if we were to resect that area, we would have a pretty significant gap.

You have raised this question to me before, and we're starting to collect some of the tissue to see whether it's ductal tissue, aortic tissue, what it is that's left behind. At this point I can't say for sure, and we just patch augment it.