Comparison of the Profiles of Postoperative Systemic Hemodynamics and Oxygen Transport in Neonates After the Hybrid or the Norwood Procedure

A Pilot Study

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Background**—**After the Norwood procedure, early postoperative neonatal physiology is characterized by hemodynamic instability and imbalance of oxygen transport that is commonly attributed to surgical myocardial injury and a systemic inflammatory response to cardiopulmonary bypass (CPB). Because the Hybrid procedure (arterial duct stenting and bilateral pulmonary artery banding) avoids CPB, cardioplegic arrest, and circulatory arrest, we hypothesized that the Hybrid procedure is associated with superior postoperative hemodynamics and oxygen transport.

Methods and Results**—**Oxygen consumption (VO_2) was continuously measured using respiratory mass spectrometry for 72 hours after Hybrid (n=6) and Norwood (n=13) procedures. Arterial, superior vena cava, and pulmonary venous blood gases and pressures were measured at 2- to 4-hour intervals to calculate systemic and pulmonary blood flows (Qs, Qp), and systemic vascular resistance (SVR), total pulmonary vascular resistance including pulmonary arterial band or B-T shunt (tPVR), cardiac output (CO), oxygen delivery (DO_2), and oxygen extraction ratio (ERO_2). Rate-pressure product was calculated as heart rate×systolic arterial pressure. When compared with the Norwood procedure, the early postoperative Hybrid patients had lower CO, higher SVR, and higher Qp:Qs ratios. In addition, the DO_2 and VO_2 were both lower in the Hybrids with higher ERO_2 and lactate levels. This early postoperative pattern reversed after 48 hours.

Conclusions**—**Although Hybrid procedure avoids CPB and cardioplegic arrest, the early hemodynamic profile is not superior to the Norwood in terms of cardiac output and control of pulmonary blood flow. These data strongly suggest that a "hands off" approach to postoperative care in Hybrid patients may not be appropriate in patients with preoperative diminished myocardial function; and in such patients a Norwood-derived management strategy (afterload reduction and inotropic support) should be considered. **(*Circulation*. 2007;116[suppl I]:I-179–I-187.)**

Key Words: cardiac output ■ cardiopulmonary bypass ■ heart defects, congential ■ hemodynamics ■ oxygen

After the Norwood procedure, many patients transition from a relatively stable preoperative status to that of profound hemodynamic instability and oxygen transport imbalance with subsequent morbidity and mortality.[1] This deterioration has been attributed to myocardial ischemia-reperfusion injury and the systemic inflammatory response to cardiopulmonary bypass (CPB). An emerging alternative to Norwood-type stage I palliation for the hypoplastic left heart syndrome, the Hybrid procedure, combines catheter-based and surgical techniques to provide neonatal palliation for these patients.[2] Catheter-based stenting of the duct allows maintenance of systemic cardiac output (Qs) after cessation of prostaglandin therapy, and surgically placed bilateral pulmonary artery bands are used to limit pulmonary blood flow (Qp) and prevent pulmonary overcirculation. By avoiding both cardioplegic arrest with the attendant myocardial dysfunction and the instability of systemic and pulmonary vascular resistance associated with CPB, it is hypothesized that the Hybrid procedure achieves superior postoperative hemodynamic stability and oxygen transport. There are, however, no published data regarding postoperative hemodynamics and oxygen transport after the Hybrid procedure.

We have recently developed a novel technique of direct continuous measurement of systemic oxygen consumption (VO_2) and intermittent measurement of arterial, pulmonary venous, and superior vena cava blood gases and pressure to assess the hemodynamics and oxygen transport after the Norwood procedure.[3,4] Consequently, we have applied this technique to compare these parameters in contemporaneous patients undergoing Hybrid and Norwood procedures.

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TABLE 1. Clinical Data for the 19 Patients

Patient	Age, days	Weight, kg	BSA, m^2	CPB, min	ACC, min	Circulatory Arrest, min	Cerebral Perfusion, min	Diagnosis
Hybrid group								
1	8	2.60	0.20					HLHS, AA, MA
2	8	3.51	0.20					HLHS, AA, MS
3	9	3.80	0.25					HLHS, AA, MS
4	25	3.74	0.23					HLHS, AA, MS
5	6	3.40	0.22					HLHS, AA, MS
6	2	2.57	0.18					HLHS, AA, MA
Norwood group								
1	7	3.5	0.23	108	47	12	35	HLHS, AS, MS
2	4	3.7	0.25	151	100	35	53	HLHS, AA, MA
3	7	4	0.26	105	47	3	44	HLHS, AA, MS
4	16	3.5	0.24	133	39	34	0	HLHS, endocardial fibroelastosis of LV, AS, MS
5	7	4.2	0.27	122	62	3	60	HLHS, AA, MS
7	6	3.5	0.23	172	82	9	70	HLHS, AS, MS
8	16	3.9	0.25	170	60	1	60	HLHS, AS, MS
9	7	4	0.25	167	64	17	44	HLHS, AS, MS
10	6	2.9	0.2	142	62	1	62	HLHS, AA, MS
11	7	2.8	0.19	66	59	17	20	HLHS, AA, MS
12	5	2.45	0.18	170	126	46	60	HLHS, AA, MS
13	4	4.19	0.27	124	99	44	49	HLHS, AS, MS, TAPVC

AA indicates aortic atresia; AS, aortic stenosis; CPB, cardiopulmonary bypass; ACC, aortic cross clamp; DILV HLHS, hypoplastic left heart syndrome; LV, left ventricle; MA, mitral atresia; MS, mitral stenosis; TAPVC, total abnormal pulmonary venous connection; TGA, transposition of great arteries; VSDs, multiple ventricular septal defects.

Materials and Methods

Patients

This study was approved by the Research Ethics Board at the Hospital for Sick Children, and written informed consent was obtained from the parents of all patients. Six neonates (3 boys, age ranged from 2 to 25 days, median 6 days) underwent Hybrid procedures. Because uniform blood sampling for systemic gas measurements was necessary and would be confounded in Hybrid patients with prograde aortic flow, enrolment in the protocol was limited to patients with aortic atresia. Norwood and Hybrid procedures were offered to all patients and the choice to undergo Hybrid palliation was based on parental and cardiologist preference. Norwood procedures were presented as the "gold standard", and Hybrid procedures were presented as a newer but unproven innovation. One patient had risk factors for a Norwood procedure including small size (2.4 kg) and mosaic Turner syndrome. Comparison was made with 13 concurrent neonates (12 boys, age ranged from 4 to 16 days, median 7) undergoing a Norwood procedure with B-T shunt. All patients underwent their surgical procedures between April 2004 and January 2006. Clinical characteristics of the patients are presented in Table 1.

Intraoperative Procedures

All patients were intubated with cuffed endotracheal tubes (Microcuff-Heidelberg-pediatric, Microcuff GmbH). General anesthesia was maintained with inhaled isoflurane, intravenous fentanyl, and pancuronium bromide. Monitoring catheters and intravascular access was generally the same for both procedures.

Hybrid Procedure

Hybrid procedures were performed in the cardiac catheterization laboratory. After median sternotomy, the left pulmonary artery was then banded with a 3-mm-long segment of PTFE conduit (3.5 mm diameter, Gore Inc) which was incised lengthwise, wrapped around the pulmonary artery, and then secured with interrupted sutures.[5,6] The right pulmonary artery was banded in a similar fashion and the patient was anticoagulated with 150u/kg heparin. To prevent loss of retrograde flow in the aortic arch after stent deployment across the aortic isthmus, a 3.5-mm PTFE shunt was anastomosed from the innominate artery to the main pulmonary artery as previously described.[7] The main pulmonary artery was cannulated and a stent (PROTÉGÉ EverFlex Self-Expanding Stent System, ev3 Inc) placed in the ductus arteriosus under fluoroscopic guidance. The location of the stent and confirmation of the pulmonary artery banding was obtained using fluoroscopic imaging to confirm creation of tight band-associated proximal branch pulmonary artery stenoses. Pulmonary vein saturations were obtained before pulmonary artery banding and in the postoperative period through an indwelling catheter in the right upper pulmonary vein. Atrial septostomy and stenting was performed in patients with restrictive atrial septal defects. Dopamine (5 μg/min/kg) was used in 3 patients before the hybrid procedure (Patients 1, 3, and 5) and was discontinued before leaving the catheterization laboratory.

Norwood Procedure

Norwood procedures were performed using low-flow CPB and selective regional cerebral perfusion as described.[8] The aortic arch was reconstructed with a homograft patch and a 3.5-mm right modified Blalock-Taussig shunt were used. All patients received methylprednisolone (30 mg/kg) before CPB. Phenoxybenzamine (0.25 mg/kg) was given at initiation of CPB. Aprotinin 50 000 KIU/kg was given followed by 100 000 KIU/100 mL prime. Milrinone (100 μg/kg) was administered before termination of CPB and dopamine (5 μg/kg/min) on cessation of CPB. Pulmonary venous lines and superior vena cava oximetric sampling lines were placed.

Postoperative Management Strategy for Norwood and Hybrid Patients

Temperature was maintained between 36°C and 37°C. Sedation consisted of a continuous infusion of morphine and lorazepam as required. Pancuronium was given for muscle relaxation. Patients received time-cycled pressure control/pressure support ventilation. Arterial oxygen saturation was maintained between 70% to 85%. Hemoglobin was maintained between 14 to 16 mg/dL. For the Norwood patients, inotropes (dopamine), vasoactive drugs (milrinone, phenoxybenzamine and vasopressin), and volume infusions (5% albumin or blood) were administered according to a standard protocol.[9] For the Hybrid patients, inotropes and vasoactive drugs were used when felt to be clinically indicated, typically on the basis of low superior vena cava oxygen saturations or low blood pressure.

Methods of Measurements

Patient Monitoring

All patients had continuous monitoring of systemic, superior vena caval, and pulmonary venous pressures, heart rates, and temperature.

Oxygen Consumption

VO_2 was measured continuously using an AMIS2000 respiratory mass spectrometer (Innovision A/S). This is a sensitive and accurate method for continuous gas analysis that allows simultaneous measurements of multiple gas fractions.[10]

Calculations of Hemodynamics and Oxygen Transport

Blood samples were taken from the arterial line, superior vena cava, and pulmonary vein lines for the measurements of blood gases and oxygen saturation. Qp and Qs were calculated using the direct Fick method. Total cardiac output (CO), systemic oxygen delivery (DO_2), systemic vascular resistance (SVR), total pulmonary vascular resistance inclusive of the Blalock-Taussig shunt in the Norwood procedure or PA bands in the Hybrid procedure (tPVR), and oxygen extraction ratio (ERO_2) were calculated. Stroke volume was calculated as CO divided by heart rate. The rate-pressure product was calculated by multiplying the heart rate by the systolic arterial pressure, as an indirect index of myocardial VO_2[11].

Study Protocol

In patients undergoing Hybrid procedures, preoperative measurement of systemic hemodynamics and oxygen transport was made after sternotomy but before pulmonary artery banding and arterial duct stenting. Both groups of patients were studied during the first 72 hours after arrival in the intensive care unit (ICU).

Data Analysis

Data are expressed as mean±SD. A paired *t* test was used to compare the variables before operation and the first measurements after the arrival in the ICU in Hybrid patients. Mixed linear regression analysis for repeated measures was used to determine the nature of any time trend over the 72-hour study period. It was also used to compare the differences in levels and trends between groups with analysis of the effects of group interaction between time and group. The parameter estimates and probability values of the group effect indicate the difference in the overall levels of each variable between the 2 groups. The parameter estimates and probability values of the interaction of time and group indicate the difference in trends of each variable between the groups. For some measures various transformations of time (logarithmic and polynomial) were tested regarding the best fit for the time course. All data analysis was performed using SAS statistical software version 9.2 (SAS Institute Inc).

The authors had full access to and take full responsibility for the integrity of the data. All authors have read and agree to the manuscript as written.

Results

Patients

There was no significant difference in age (10±8 and 7±3 days, $P>0.05$) and body weight (3.3±0.6 and 3.7±4.9 kg, $P>0.05$) between the Hybrid and Norwood groups. Body surface area was significantly less in the Hybrid patients as compared with the Norwood patients (0.21±0.03 and 0.24±0.03 m^2, $P=0.045$).

TABLE 2. Preoperative and the First Postoperative Measures of Systemic Hemodynamics and Oxygen Transport in 6 Neonates Undergoing the Hybrid Procedure

	Preoperative Measures	1st Postoperative Measures in the ICU	*P* Values
Temperature	34.9±0.8	35.8±0.4	0.049
Heart rate, beat/min	142±7	150±9	0.26
SAP, mm Hg	56±3	76±16	0.11
DAP, mm Hg	33±7	34±5	0.73
MAP, mm Hg	42±9	48±12	0.16
RPP	7932±1210	9791±2438	0.09
SVR, Wood unit×m^2	21.1±12.2	45.8±14.5	0.0001
tPVR, Wood unit×m^2	9.6±6.1	25.8±8.0	<0.0001
Qs, L/min/m^2	2.0±0.9	0.9±0.2	0.03
Qp, L/min/m^2	4.3±1.7	1.7±0.3	0.009
CO, L/min/m^2	6.3±2.2	2.6±0.4	0.009
Qp:Qs	2.5±1.4	1.8±0.5	0.16
Stroke volume, ml/beat per m^2	209±67	81±14	0.006
PaO_2, mm Hg	49.1±12.6	41.3±3.0	0.11
SaO_2, %	84±11%	77±6	0.07
Hb, g/dL	12.5±1.2	17.0±1.1	<0.0001
DO_2, ml/min/m^2	287±138	168±35	0.065
VO_2, ml/min/m^2	72±12	76±23	0.48
ERO_2	0.29±0.12	0.46±0.13	0.008
Lactate, mmol/L	1.5±0.3	3.5±2.0	0.049

DAP indicates diastolic arterial pressure; DO_2, systemic oxygen delivery; ERO_2, oxygen extraction ratio; Hb, hemoglobin; MAP, mean arterial pressure; PaO_2, arterial oxygen tension; Qp, pulmonary blood flow; Qs, systemic blood flow; RPP, rate-pressure produce; SaO_2, arterial oxygen saturation; SAP, systolic arterial pressure; SVR, systemic vascular resistance; rPVR, total pulmonary vascular resistance inclusive of pulmonary arterial bands; VO_2, systemic oxygen consumption.

Hybrid Patients

Patients were extubated between 1 to 8 days after surgery (median 6 days). Milrinone (0.66 to 0.99 μg/kg/min) was used in 4 of 6 the patients in the early postoperative period. Phenoxybenzamine (1.0 to 1.5 mg/d per kg) was administered in 1 patient (Patient 5) at 14 hours after the arrival in the ICU and terminated after 72 hours. Nitroprusside (2 to 3 μg/kg/min) was used in another patient (Patient 4) from postoperative hours 6 to 28. Dopamine (5 to 10 μg/min per kg) was administered to 3 patients at 6 hours after the procedure and continued for 8 to 30 hours (Patients 1, 2, and 5).

None of the Hybrid patients died during the study period. One patient required atrial stenting after the conclusion of the study period which was complicated by entanglement with tricuspid valve chordae and subsequent reoperation, ECMO, and death. Another patient died on postoperative day 53 after requiring ECMO support for fulminant adenoviral pneumonitis. One patient (Patient 4) who underwent the Hybrid

TABLE 3. Statistical Analysis Results of the Changes of Systemic Hemodynamics and Oxygen Transport in Relation to Time During the 72-Hour Study Period in the 6 Neonates Following the Hybrid Procedure

Variables	Intercept	Estimate Parameter	P Values
Temperature, °C	36.5	0.006	0.01
Heart rate, beat/min	168	−0.20	<0.0001
SAP, mm Hg	64	0.21	<0.0001
DAP, mm Hg	33	0.11	<0.0001
MAP, mm Hg	44	0.13	<0.0001
RPP, unit	10671	21.9	<0.0001
SVR, Wood unit×m^2*	44.3	−6.0	<0.0001
tPVR, Wood unit×m^2	20	−0.08	0.001
Qs, L/min/m^2	0.98	0.03	<0.0001
Qp, L/min/m^2	1.8	0.015	<0.0001
Qp:Qs	2.0	−0.013	<0.0001
CO, L/min per m^2	2.8	0.04	<0.0001
Stroke volume, ml/beat per m^2	81	1.48	<0.0001
PaO_2, mm Hg	41.2	0.04	0.01
SaO2, %	76.8	0.03	0.10
Hb, g/dL	15.0	−0.027	<0.0001
DO_2, ml/min/m^2	155	4.2	<0.0001
VO_2, ml/min/m^2	71.8	0.29	<0.0001
ERO_2*	0.54	−0.07	<0.0001
Lactate, mmol/L*	4.7	−0.73	<0.0001

Abbreviations are as indicated in Table 2.
*Data were entered after logarithmic transformation.

procedure for intended pretransplant palliation was discharged home and returned for successful heart transplantation on postoperative day 60.

Norwood Patients

All patients were extubated between 4 to 16 days after surgery (median 7 days). The duration of intubation was longer in the Norwood patients as compared with the Hybrid patients (11±6 and 5±2 days, respectively, $P=0.026$). Milrinone (0.33 to 0.99 μg/min/kg) was used in all Norwood patients throughout the study period. Phenoxybenzamine (0.5 to 2.0 mg/d per kg) was commenced within the first 14 hours and continued for the remainder of the study period in all Norwood patients. Vasopressin (0.0001 to 0.0005 U/min/kg) was given in 7 patients at different times during the study period. Dopamine (5 μg/min/kg) was used in 8 of the patients preoperatively and was initiated before the termination of CPB in all patients (5 to 10 μg/kg/min), and subsequently stopped within the first 24 hours after arrival in the ICU in 10 patients, and at 40 to 52 hours in 2 patients, and for the entire study period in the remaining patient. One patient required ECMO support after completion of the study period. There were no in-hospital deaths among the Norwood patients.

Postoperative Profiles of Hemodynamics and Oxygen Transport in Hybrid Patients

Tables 2 and 3 and Figure 1 show the results of the trends of central body temperature, hemodynamics, and oxygen transport in the Hybrid group.

Perioperative Changes in Hemodynamics and Oxygen Transport

Comparison of preoperative and the first postoperative measures on arrival in the ICU showed a significant increase in central temperature ($P<0.05$) and insignificant increase in heart rate, systolic, diastolic and mean arterial pressures ($P>0.05$). There was a significant increase in SVR ($P=0.0001$) and tPVR ($P<0.0001$) and a significant decrease in Qs ($P=0.03$), Qp ($P=0.009$) and CO ($P=0.009$). There was a decrease in the ratio of Qp:Qs, PaO_2, and SaO_2 although not achieving statistical significance ($P>0.05$ for all). Hb increased significantly ($P<0.0001$). DO_2 decreased but did not reach statistical significance ($P=0.065$). VO_2 did not change significantly ($P=0.48$), but ERO_2 increased significantly ($P=0.008$). Arterial lactate increased significantly ($P=0.049$) (Table 2 and Figure 1).

Postoperative Hemodynamic and Oxygen Transport

Central temperature increased over the 72 hours after arrival in the ICU ($P=0.01$). All hemodynamic and oxygen transport variables showed substantial interindividual and intraindividual variations over the study period. Heart rate linearly decreased over the study period ($P<0.0001$). Arterial blood pressure (systolic, diastolic, and mean; $P<0.0001$ for all) and rate-pressure product increased linearly over time ($P<0.0001$). SVR was significantly related to time after logarithmic transformation and showed a rapid decrease in the first 24 hours ($P<0.0001$). tPVR linearly decreased over time ($P=0.001$). Qs, Qp, CO, and stroke volume increased significantly over time ($P<0.0001$). There was no significant change in SaO_2 ($P=0.10$), but a significant increase in PaO_2 ($P=0.01$) and a significant decrease in Hb over time ($P<0.0001$). There was a significant increase in DO_2 ($P<0.0001$) and a small increase in VO_2 over time ($P<0.0001$). As a result, ERO_2 decreased and was related to time after logarithmic transformation, decreasing most rapidly in the first 24 hours. Arterial lactate was also related to time after logarithmic transformation; decreasing rapidly in the first 24 hours (Table 3 and Figure 1).

Postoperative Profiles of Hemodynamics and Oxygen Transport in Norwood Patients

Table 4 and Figure 1 show the results of the trends of central body temperature, hemodynamics, and oxygen transport in Norwood groups. The details of the profiles have been described in our previous study.[6]

Comparison of Postoperative Profiles of Hemodynamics and Oxygen Transport Between the Hybrid and the Norwood Procedures

There was no difference in temperature between the 2 groups of patients during the first 72 hours ($P=0.97$), but the trends were significantly different with a significant interaction between time and group ($P=0.01$) and a small increase in Hybrid patients but nonsignificant change in the Norwood

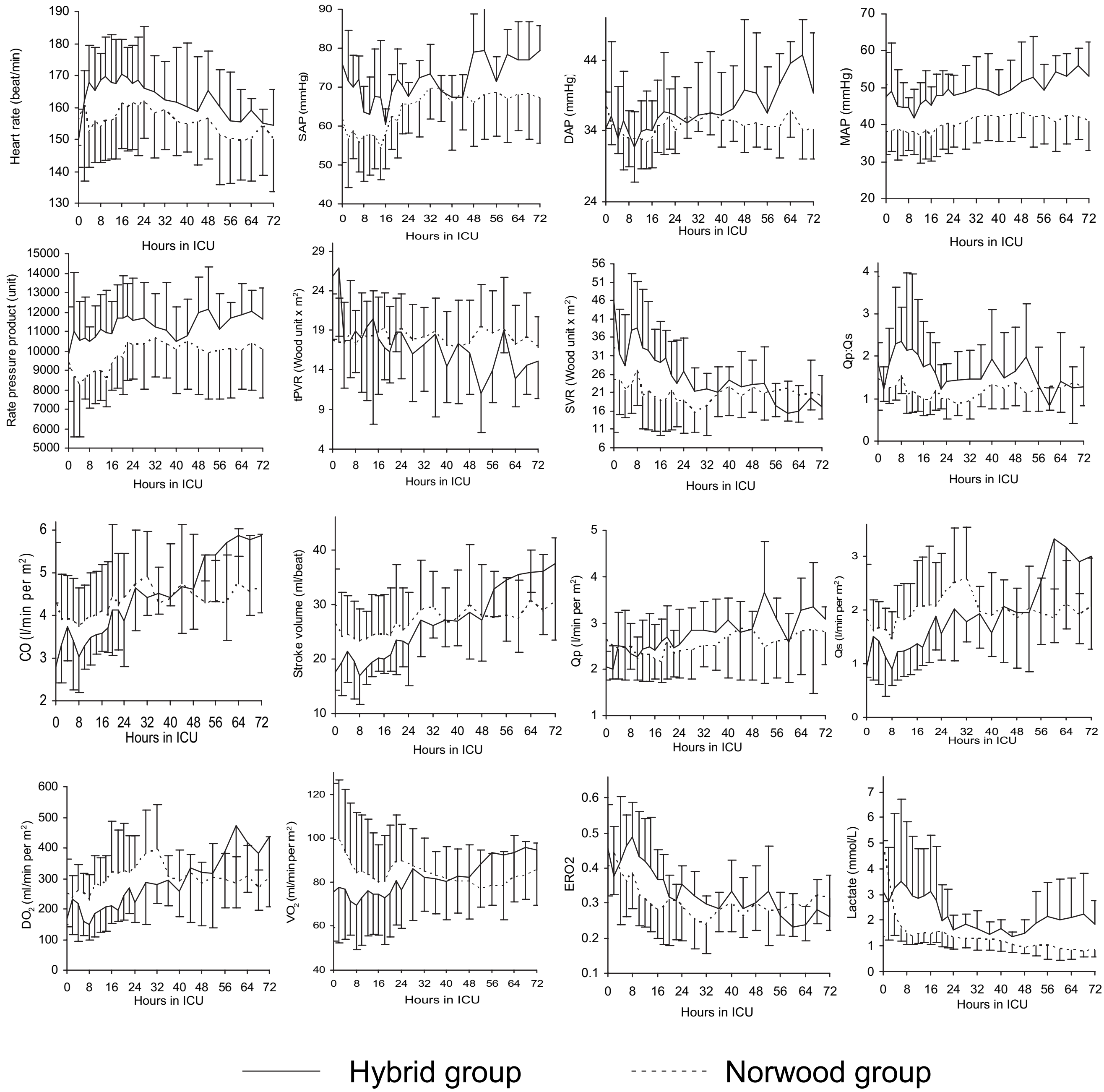

Figure 1. Hemodynamics and oxygen transport parameters after Hybrid (n=6; solid line) and Norwood procedures (n=13; dotted line) including heart rate, blood pressures, rate-pressure product, total pulmonary vascular resistance including the resistance of the pulmonary arterial banding or BT shunt (tPVR) and systemic vascular resistances (SVR), pulmonary (Qp) and systemic blood flows (Qs), and Qp:Qs, total cardiac output (CO), stroke volume, oxygen delivery (DO2), oxygen consumption (VO_2), oxygen extraction ratio (ERO2).

patients. Heart rate tended to be higher in Hybrid patients ($P=0.09$) with a similar decreasing trend over time ($P=0.22$). Systolic arterial pressure tended to be higher in Hybrid patients but the difference did not achieve statistical significance ($P=0.29$). There was no significant deference in diastolic arterial pressure between the 2 groups ($P=0.61$) but the Hybrid patients showed a faster increase over the 72 hours ($P<0.0001$). Thus mean arterial pressure was higher ($P=0.03$) and increased faster ($P<0.0001$) in Hybrid patients as compared with the Norwood patients. Rate-pressure product tended to be higher in the Hybrid patients ($P=0.063$) with similar trends in the two groups ($P=0.95$) (Table 5 and Figures 1 and 2).

SVR was initially higher and more rapidly decreased in Hybrid patients ($P<0.0001$) reaching a level similar to the Norwood patients after 36 hours. In the Hybrid patients, tPVR increased from 9.6±6.1 to 25.8±6.0 Wood unit×m^2 and SVR increased from 21.1±12.2 to 45.8±14.5 Wood unit×m^2 (pre- versus postoperative). In contrast, postoperative Norwood tPVR and SVR were 17.7±5.8 and 24.5±14.2 Wood unit×m^2 respectively. Qs was initially lower in the Hybrid patients ($P<0.001$) and increased more rapidly

TABLE 4. Statistical Analysis of the Changes of Systemic Hemodynamics and Oxygen Transport in Relation to Time During the 72 Hour Study Period in the 13 Neonates Following the Norwood Procedure

Variables	Intercept	Estimate Parameter	*P* Values
Temperature, °C	36.5	0.0001	0.89
Heart rate, beat/min	159	−0.1	0.0001
SAP, mm Hg	58	0.17	<0.0001
DAP, mm Hg	34	0.16	0.04
MAP, mm Hg	38	0.07	<0.0001
RPP, unit	9006	22	<0.0001
SVR, Wood unit*m²*	21.6	−0.02	0.15
tPVR, Wood unit*m²	18.1	−0.001	0.87
Qs, L/min/m²**	1.6	Time 0.026	<0.0001
		Time² −0.0003	0.0002
Qp(L/min/m²	1.9	0.006	<0.0001
Qp:Qs	1.2	0.0006	0.61
CO, L/min/m²*	3.3	0.26	<0.0001
Stroke volume, ml/beat/m²	114	0.4	<0.0001
PaO_2, mm Hg*	32.2	2.7	<0.0001
SaO2, %*	68.6	2.1	<0.0001
Hb, g/dL	15.3	−0.02	<0.0001
DO_2, ml/min/m² **	239	Time4.8	<0.0001
		Time²−0.06	<0.0001
VO_2, ml/min/m²	96.6	−3.9	<0.0001
ERO_2*	0.42	−0.037	<0.0001
Lactate, mmol/L*	3.4	−0.54	<0.0001

Abbreviations are as indicated in Table 2.

*Data were entered after logarithmic transformation; **after polynomial transformation, with time indicating the coefficient of the early trend, and time² indicating the later trend.

($P<0.0001$) to reach a level similar to the Norwood patients at approximately 36 hours and thereafter remained higher than the Norwood patients. There was no significant difference in the levels of tPVR and Qp between the groups, but a faster decrease in tPVR and increase in Qp were noted in the Hybrid patients as compared with the Norwood patients (Figure 1). Qp:Qs was significantly higher ($P=0.003$) and diminished faster ($P<0.0001$) in the Hybrid patients as compared with the Norwood patients (Figure 1). Qp:Qs ranged from 0.36 to 5.7 (mean: 1.7±1.0) in the Hybrid patients. Among these values, a Qp:Qs more than 2.0 and less than 3.0 occurred in 17% of the measurements (22 of 132 measurements), and Qp:Qs >3 in 11% (14 measurements) (Figure 2A). In comparison, in the Norwood patients, Qp:Qs ranged from 0.3 to 3.3 (mean: 1.2±0.5), and Qp:Qs >2.0 occurred in 5% of the measurements (16 of 325 measurements), and only 1 measurement was >3.0 (Figure 2B).

CO and stroke volume were lower ($P=0.005$ and $P=0.03$, respectively) but with a significantly faster recovery ($P<0.0001$ for both) in the Hybrid patients and reached a level similar to the Norwood patients after 36 hours and thereafter was greater than the Norwood patients. PaO_2 and SaO_2 were significantly higher ($P=0.002$ and $P=0.01$, respectively) but with a slower increase in Hybrid patients as compared with the Norwood patients ($P<0.0001$ and $P=0.03$, respectively). There was no significant difference in Hb between the 2 groups. DO_2 was lower ($P<0.0001$) with a significantly faster recovery ($P<0.0001$) in the early postoperative Hybrid patients and became higher than the Norwood patients after 48 hours. VO_2 was lower ($P=0.002$), with a rapid increase over the study period in the Hybrid patients. In the Norwood patients, VO_2 showed a significant decrease over time in a logarithmic fashion. VO_2 was higher in the Hybrid patients at 48 hours. ERO_2 was higher throughout the study period ($P=0.0008$) despite a faster decrease ($P=0.002$) in Hybrid patients. Arterial lactate was not different between the groups (Figure 1).

Discussion

This is the first study describing the early postoperative hemodynamic and oxygen transport responses to the Hybrid procedure for palliation of hypoplastic left heart syndrome. Despite avoidance of CPB, cardioplegic arrest, and circulatory arrest, the Hybrid procedure was characterized by diminished oxygen delivery, higher systemic vascular resistance, and higher oxygen extraction ratio despite lower oxygen consumption when compared with Norwood patients. These data demonstrate previously unmeasured hemodynamic consequences associated with the Hybrid procedure and suggest that early postoperative management of the Hybrid patients (especially those with diminished myocardial function) could be improved with afterload reduction and inotropic support. Despite the initial observed deficits, however, the Hybrid patients rapidly recovered, and by 48 hours the relative pattern of hemodynamic compromise was reversed with more favorable hemodynamics in the Hybrid patients.

The Norwood and Hybrid procedures share common objectives. Both are designed to provide unobstructed Qs by aortic arch reconstruction (Norwood) or ductal stenting (Hybrid) and to limit Qp with a modified B-T shunt (Norwood) or bilateral pulmonary artery banding (Hybrid). These maneuvers are designed to stabilize the hemodynamic status of a newborn with hypoplastic left heart syndrome until second stage palliation can be performed. Because achievement of these objectives in the Norwood patients requires CPB, cardioplegic arrest, and some form of altered cerebral perfusion, postoperative instability has been commonly attributed to sequelae of these surgical maneuvers including ischemia-reperfusion injury and the effects of the systemic inflammatory response to CPB (eg, secondary myocardial dysfunction, vasomotor instability, and increased VO_2).[3,12] Management of the "post-Norwood" circulation has evolved over the past 2 decades with manipulation of the SVR now being seen as an important variable in maintaining adequate Qs and DO_2.[9,13]

By avoiding CPB-associated injury, the Hybrid procedure is hypothesized to lead to a reduced inflammatory response and superior cardiovascular performance in the early postoperative period. In the current study, the "hypermetabolic state" of the postoperative Norwood patient (and patients after CPB in general) is manifest by an elevated early postoperative VO_2[3,10,14,15] and contributes to impaired balance of oxygen transport.[3] In contrast, the lower VO_2 after Hybrid

TABLE 5. Statistical Results of the Comparison of the Changes of Systemic Hemodynamics and Oxygen Transport During the 72-Hour Study Period Between the Hybrid and Norwood Groups

	Time		Group		Time×Group	
Variables	Estimate Parameter	*P* Value	Estimate Parameter	*P* Value	Estimate Parameter	*P* Value
Temperature, °C	0.006	0.006	0.007	0.97	0.007	0.01
Heart rate, beat/min	−0.17	0.0002	0.86	0.09	−0.06	0.22
SAP, mm Hg	0.28	<0.0001	5.93	0.29	0.039	0.24
DAP, mm Hg	0.11	<0.0001	−0.46	0.79	0.09	<0.0001
MAP, mm Hg	0.13	<0.0001	6.9	0.03	0.06	<0.0001
RPP, unit	21.9	<0.0001	1663	0.063	−0.38	0.95
tPVR, Wood unit×m^2	−0.08	<0.0001	2.33	0.27	−0.08	0.0003
SVR, Wood unit×m^2*	−6.1	<0.0001	20.9	<0.0001	−5.2	<0.0001
Qp, L/min/m^2	0.015	<0.0001	0.085	0.75	0.008	0.0008
Qs, L/min/m^2*	0.50	<0.0001	−1.60	0.001	0.36	<0.0001
CO, L/min/m^2*	0.80	<0.0001	−1.6	0.005	0.53	<0.0001
Qp:Qs	−0.013	<0.0001	0.82	0.003	−0.014	<0.0001
Stroke volume, ml/beat/m^2	1.44	<0.0001	−34.4	0.03	1.04	<0.0001
PaO_2, mm Hg*	1.12	0.001	6.98	0.002	−1.59	<0.0001
SaO2, %*	4.0	<0.0001	6.6	0.01	−1.25	0.03
Hb, g/dL	−0.10	<0.0001	8.62	0.09	−0.06	0.22
DO_2, ml/min/m^2*	73.7	0.0001	−191.1	0.0009	55.2	<0.0001
VO_2, ml/min/m^2	5.3	0.0001	−32.7	0.002	9.2	<0.0001
ERO_2*	−0.07	<0.0001	0.12	0.008	−0.03	0.002
Lactate, mmol/L*	−0.03	<0.0001	0.77	0.09	−0.006	0.21

Abbreviations are as indicated in Table 2.

*Data were entered after logarithmic transformation.

Parameter estimate of group effect indicates the difference in the overall levels of each variable between the 2 groups: '+' indicates a higher level, and '−' indicates a lower lever in the Hybrid group as compared to the Norwood group.

The parameter estimates of the interaction of time and group indicate the difference in trends of each variable between the groups. '+' indicates a faster increase, and '−' indicates a faster decrease in Hybrid group as compared to Norwood group

procedure (possibly attributable to avoidance of CPB) is advantageous as it compensates for the lower DO_2 seen in these patients. This benefit, however, was only partial and overall the balance of delivery and consumption (ERO_2) in the first 48 postoperative hours was diminished in the Hybrid group.

The observed increased ERO_2 in the Hybrid patients suggest limited myocardial reserve. This decrement in myocardial performance may be attributable to a similar hemodynamic burden placed on the right ventricle with either of the 2 operative approaches. Specifically, the construction of modified B-T shunt (in the Norwood procedure) or bilateral pulmonary artery bands imposes an acute pressure load to an already volume loaded single right ventricle. Animal and human data from normal biventricular circulation have shown undesirable responses to pulmonary artery or aortic banding with myocardial injury and reduced contractility,[16–18,19,20] The neonatal single right ventricle might be disadvantaged in its ability to respond to acute increase in afterload, resulting in a reduction in total cardiac output. Additionally, acute pressure loading in animal subjects with biventricular circulation has been found to be associated with increased circulating levels of rennin, angiotensin, and catocholamines.[21,22] Postoperative elaboration of circulating vasoconstrictors may further increase the SVR after Hybrid (or

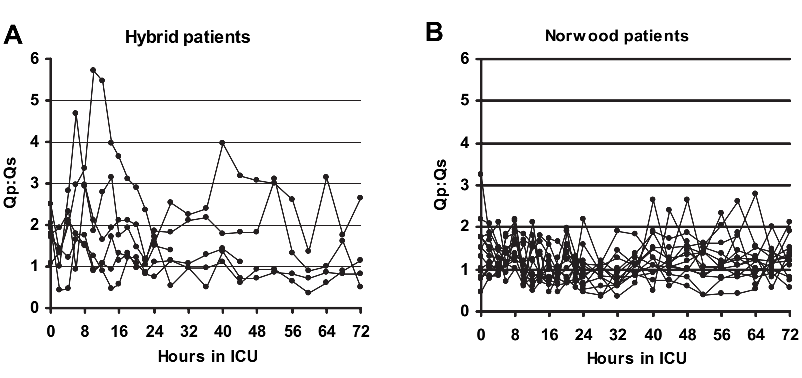

Figure 2. Qp:Qs in neonates during the first 72 hours after (A) Hybrid (n=6) and (B) Norwood (n=13) procedures.

Norwood) procedures and thereby contribute to reductions in CO and DO_2. Thus our "hands off" approach to postoperative Hybrid management may be inappropriate in patients with diminished preoperative myocardial performance.

It is important to note that these postoperative measurements were obtained after intraoperative administration of phenoxybenzamine and milrinone in all of the Norwood patients, whereas intraoperative vasodilators and inotropes were uncommonly used during and after the Hybrid procedures. Consequently, the superior DO_2 in the Norwood patients may simply reflect the different management strategy used (eg, inotropic and vasodilatory support) rather than an important deficit in the myocardial function of Hybrid patients. The diminished myocardial performance in the early postoperative Hybrid patients may be related to increased SVR attributable to endogenous release of catecholamines,[21,23] which was specifically treated in the Norwood patients (phenoxybenzamine) but not treated in the Hybrid patients. Whereas the inferior myocardial performance in the Hybrid patients did not have overt clinical consequences (mortality, ventilation time, ICU stay), it may be possible to accelerate recovery by manipulation of the adverse hemodynamics (increased SVR and decreased Qs) by use of vasodilator strategies developed for postoperative Norwood patients.

Another important finding in the present study was the relatively high Qp:Qs ratios in the Hybrid patients despite the presence of bilateral pulmonary artery bands. Although this, in part, may be related to the aforementioned elevation of SVR, it is important to note that the presence of bilateral pulmonary artery bands did not eliminate the potential for pulmonary overcirculation with Qp:Qs ratios that frequently exceeded 2.5:1. Consequently, the benefit of the Hybrid procedure may reside in the avoidance of high VO_2 states rather than tight control of Qp. Quantitative evaluation of Qp:Qs measurements has not been previously reported, and recognition of this potential for pulmonary overcirculation is important as there are several medical methods at the clinician's disposal to control Qp through ventilatory management and systemic afterload reduction.

Conclusions

Despite the absence of CPB, cardioplegic arrest, and circulatory arrest, the early postoperative Hybrid patient (in whom minimal inotropic or vasodilatory support has been used) has less favorable overall circulatory performance when compared with postoperative Norwood patients in whom inotropic and vasodilatory support is routinely used. Although this early deficit is well-tolerated and rapidly reversed, it suggests that the early postoperative Hybrid patient may undergo a period of limited myocardial reserve and clinical awareness of this pattern of recovery may be of benefit to the clinician—especially in those patients with preoperative deficits in myocardial performance. In patients undergoing a hybrid procedure with known preoperative myocardial dysfunction, the routine use of postoperative inotropic and vasodilatory support (as commonly used after a Norwood procedure) should be strongly considered. In addition, the Qp:Qs can be high in the postoperative Hybrid patients and the presence of bilateral pulmonary artery bands should not be considered as complete protection against pulmonary overcirculation.

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Disclosures

None.

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