Inhaled Nitric Oxide Use in Bidirectional Glenn Anastomosis for Elevated Glenn Pressures

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Background. **Children frequently undergo bidirectional Glenn anastomosis in the staged surgical management of single ventricle physiology. The purpose of our study was to investigate the role of inhaled nitric oxide therapy in children with marked elevations in Glenn pressures after this surgery.**

Methods. **A retrospective study over a 30-month period was performed. The effect of inhaled nitric oxide therapy was analyzed in children with marked elevations of Glenn pressures resulting in decreased systemic perfusion. Effects on Glenn pressures, respiratory indices, and systemic perfusion were evaluated after initiation of nitric oxide therapy and compared with baseline parameters.**

Results. **Sixteen patients were placed on nitric oxide therapy for marked elevations of Glenn pressures (22.4 ± 3.9 mm Hg). In the 11 responsive patients, there were significant reductions in Glenn pressures (from 22.4 mm Hg to 17.1 mm Hg, $p < 0.001$) and significant improvement in partial pressure of oxygen to fraction of inspired oxygen ratio (from 49 to 74.3, $p = 0.001$) and oxygenation index (from 17 to 12, $p = 0.005$). There was simultaneous significant reduction in inotrope score (from 14.9 to 11.4, $p < 0.001$) and fluid volume support (from 11.4 mL/kg to 2.3 mL/kg, $p < 0.001$) in the responsive patients. Five patients that failed to show any response were found, subsequently, to have an anatomic lesion.**

Conclusions. **Inhaled nitric oxide produces significant reduction in Glenn pressures and improvement in systemic perfusion and pulmonary gas exchange in patients with marked elevations of Glenn pressures after bidirectional Glenn anastomosis. Patients who fail to respond should be investigated for an anatomic lesion.**

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The bidirectional Glenn anastomosis (BDG) is an operation that diverts systemic venous blood from the superior vena cava to both lungs, thereby providing effective pulmonary blood flow in children with single ventricle physiology. This procedure, based on initial experimental work of Carlon and colleagues [1] and subsequently performed for the first time by Haller and colleagues [2] in 1966, has become a well-defined procedure in the staged surgical management of children with single ventricle physiology. However, some of these children demonstrate postoperative complications, including elevated Glenn pressures, superior vena cava syndrome [3], and low systemic oxygen saturations [4], despite preoperative evaluations including cardiac catheterization. Inhaled nitric oxide (*i*NO), a selective pulmonary vasodilator, may have a therapeutic role in the immediate postoperative period in these patients. Evidence for use of *i*NO postoperatively in children undergoing BDG is limited with equivocal results [5–8]. The aim of the present study was to review our experience of *i*NO therapy in children undergoing BDG with marked elevations in Glenn pressures.

Material and Methods

A retrospective study was conducted in the pediatric cardiac intensive care unit of the Monroe Carell Jr. Children's Hospital at Vanderbilt. Institutional Review Board approval was obtained on May 5, 2002 and patient consent was waived for the study. Chart review of all patients who had undergone BDG over a period of two and half years from August 2000 to January 2003 was undertaken. Demographic characteristics such as age, weight, and sex, preoperative cardiac defect, and baseline oxygen saturations were noted. Preoperative cardiac catheterization results were examined for pulmonary artery pressure and pulmonary vascular resistance. Operative records were reviewed for cardiopulmonary bypass time, aortic cross-clamp time, and surgical procedures. Postoperative transesophageal echocardiography was reviewed for pressure gradient or stenosis across the Glenn shunt.

Postoperatively, Glenn pressures were recorded in all patients. The Glenn pressures were measured in the patients on the ventilator as they were placed on low

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positive end expiratory pressure (PEEP) of 0–2 cm of water (H_2O). Marked elevation of Glenn pressures was defined as elevated Glenn pressures (~ 20 mm Hg) in association with decreased systemic perfusion and hemodynamic instability. Patients with marked elevation of Glenn pressures were placed on *i*NO therapy. The *i*NO was delivered to the patient as a continuous flow into the inspiratory limb of the ventilatory circuit (INOVENT; GE Healthcare, UK). A microprocessor-controlled system allowed 1 to 80 parts per million (ppm) NO delivery and a chemiluminescence method (Pulmonox system; Messer Griesheim, Vienna, Austria) continuously measured NO and nitrogen dioxide in the circuit. Patients were initially placed on 20 ppm of *i*NO and increased to 40 ppm if they failed to respond, as evidenced by no significant reduction in Glenn pressures. Patients were labeled as nonresponders if no response was seen at 40 ppm. Further evaluation, including echocardiography and cardiac catheterization, was undertaken in nonresponders to rule out anatomic lesions. Patients were labeled as responders to *i*NO if they demonstrated a reduction in Glenn pressures and an improvement in systemic perfusion. The *i*NO was weaned in the responsive patients as per institutional weaning protocol after 1 hour of stabilization. All patients were mechanically ventilated using synchronized intermittent mandatory ventilation with pressure control and pressure support mode of ventilation on Servo 300A ventilators (Siemens-Elema AB, Solna, Sweden). Patients were initially placed on low PEEP (0–2 cm H_2O) and 8–10 mL/kg tidal volume breaths. Mechanical ventilation and oxygen therapy were based on maintenance of oxygen saturation between 80% and 85% and normal partial pressure of carbon dioxide ($Paco_2$). Sedation was used very judiciously in our patient population and pressure support ventilation was encouraged. Patients were rapidly weaned and extubated after their initial stabilization and improvement in systemic perfusion to encourage spontaneous ventilation. Continuous infusions of dopamine, dobutamine, epinephrine, and milrinone for inotrope support and crystalloid solutions for fluid volume resuscitation were administered, respectively, when necessary. Indication for inotrope usage and fluid volume support were at the discretion of the bedside physician to maintain adequate systemic perfusion based on blood pressure, heart rate, Pao_2 levels, and base deficit.

To analyze systemic perfusion, the heart rate, systemic blood pressure, inotrope score [9], fluid volume resuscitation, and base deficit of all patients receiving *i*NO therapy was studied. To analyze the effect of *i*NO therapy on pulmonary gas exchange, ventilator parameters such as PEEP, peak inspiratory pressure (PIP), inspiratory time, respiratory rate, and fraction of inspired oxygen (Fio_2) were noted. Arterial blood gas samples were analyzed for partial pressure of oxygen (Pao_2), $Paco_2$, oxygen saturation, and base deficit. Partial pressure of oxygen to fraction of inspired oxygen ratio (Pao_2/Fio_2) and oxygenation index (OI) (OI = mean arterial pressure × Fio_2/Pao_2) were calculated based on the above parameters. The effect of *i*NO therapy in all patients with elevated Glenn pressures were evaluated 1 hour and 3 hours after initiation of *i*NO therapy.

The results were analyzed using the statistical software SPSS (SPSS Inc, Chicago, IL) and R (www.r-project.org). All continuous results are expressed as mean ± standard deviation. A χ^2 or Fisher's exact test were used for categorical comparisons. The response to *i*NO therapy was studied at 1 hour and 3 hours after initiation of *i*NO therapy in comparison with baseline values before starting *i*NO therapy by means of the 2-tailed paired *t* test or the Wilcoxon signed rank test.

Results

A bidirectional Glenn anastomosis was performed in 44 infants over a period of 30 months (Table 1). Sixteen patients received *i*NO therapy in the immediate postoperative period for marked elevations in Glenn pressures (22.4 ± 3.9 mm Hg). The *i*NO was initiated within 3 hours of surgery in the operative room coming off cardiopulmonary bypass or in the intensive care unit in all 16 patients. Patients with marked elevation of Glenn pressures had significant elevation of preoperative pulmonary artery pressure ($p = 0.001$) and pulmonary vascular resistance ($p = 0.006$). No significant difference in the demographic characteristics, preoperative baseline oxygen saturation, and preoperative cardiac lesions was seen in these patients (Table 1). No significant difference was observed in the operative details of patients requiring *i*NO therapy for elevated Glenn pressures. Fourteen of 16 patients requiring *i*NO therapy underwent additional cardiac surgery: 5 patients underwent pulmonary artery reconstruction, 2 patients had a Damus-Kaye-Stansel procedure, 2 patients had a bilateral bidirectional Glenn procedure, 2 patients had ligation of the left superior vena cava, 1 patient had left atrial reduction, 1 patient had partial anomalous pulmonary venous return correction, and 1 patient had a pulmonary valvectomy. A Blalock-Taussig shunt was preserved in 3 patients to improve oxygenation. A longer cardiopulmonary bypass time was seen in the group of 16 patients receiving *i*NO although it did not reach statistical significance ($p = 0.062$) (Table 1).

Eleven patients (69%) had a positive response to *i*NO therapy as seen by a significant reduction in the Glenn pressures ($p = 0.006$ at 1 hour and $p < 0.001$ at 3 hours post therapy). Patients with marked elevation of Glenn pressures had a higher inotrope score ($p < 0.001$), required greater fluid volume support to maintain their systemic perfusion ($p < 0.001$), and had a higher negative base deficit ($p = 0.019$) (Table 2). After initiation of *i*NO therapy there was a significant reduction in inotrope score ($p < 0.001$ at 1 and 3 hours), the need for fluid volume resuscitation ($p = 0.003$ at 1 hour and $p = 0.001$ at 3 hours), and an improvement in the base deficit ($p = 0.002$ at 1 hour and $p = 0.006$ at 3 hours) (Table 3). On evaluation of the respiratory indices, there was a significant improvement in the Pao_2/Fio_2 ratio ($p = 0.002$ at 1 hour and $p = 0.001$ at 3 hours) and a significant reduction of OI ($p = 0.003$ at 1 hour and $p = 0.005$ at 3 hours) after

Table 1. Preoperative and Operative Data of Patients Undergoing BDG

	Patients on *i*NO Therapy (n = 16)	Patients Without *i*NO Therapy (n = 28)	*p* Value
Demographic characteristics			
Age (months)[a]	7.0 ± 3.1	6.2 ± 2.5	0.341
Weight (kilograms)[a]	6.4 ± 1.1	6.2 ± 1.7	0.753
Sex (M/F)	11/5	16/12	0.480
Preoperative oxygen saturations[a]	72.6 ± 4.7	75 ± 5.1	0.139
Preoperative cardiac lesion[b]			
Hypoplastic left heart syndrome	7/16	11/28	0.10
Tricuspid atresia	2/16	3/28	0.10
Ebstein anomaly	1/16	0/28	0.10
Pulmonary stenosis-atresia	5/16	7/28	0.10
Mitral atresia	0/16	1/28	0.10
Unbalanced AV canal	1/16	2/28	0.10
Double outlet right ventricle	0/16	2/28	0.10
Double inlet left ventricle	0/16	2/28	0.10
Preoperative catheterization			
MPAP (mm Hg)[a]	17.5 ± 4.0	13.3 ± 3.4	0.001
PVR (Woods units × meter^2)[a]	2.6 ± 1.1	1.8 ± 0.8	0.006
Operative details			
Cardiopulmonary bypass time (minutes)[a]	93.2 ± 34.2	72.8 ± 28.6	0.062

[a] Mean ± standard deviation. [b] Absolute number of patients.

AV = atrioventricular; BDG = bidirectional Glenn anastomosis; *i*NO = inhaled nitric oxide; M/F = male/female; MPAP = mean pulmonary artery pressure; n = total number of patients; PVR = pulmonary vascular resistance.

initiation of *i*NO therapy in the 11 responsive patients (Table 4). No significant reduction of $Paco_2$ was observed at 3 hours of therapy ($p = 0.35$).

Five patients failed to show a therapeutic response to *i*NO therapy as evidenced by no reduction of their elevated Glenn pressures. All 5 patients had elevated preoperative pulmonary vascular resistance and one patient had Blalock-Taussig shunt. All of these patients were subsequently found to have a hemodynamically significant anatomic lesion (Table 5). All 5 patients required a second operative procedure with 4 patients surviving.

Comment

In our study *i*NO therapy produced a statistically significant reduction in Glenn pressures, correlating with an improvement in systemic perfusion postoperatively in children undergoing BDG. Glenn pressures fell from 22.4 mm Hg to 19.1 mm Hg at 1 hour and 17.1 mm Hg at 3

Table 2. Immediate Postoperative (Prior to iNO Therapy) Data of Patients

	Patients on *i*NO Therapy (n = 16)[a]	Patients Without *i*NO Therapy (n = 28)[a]	*p* Value
Glenn pressure (mm Hg)	22.4 ± 3.9	15.7 ± 2.6	0.001
Heart rate	159.4 ± 16.7	151.5 ± 16.6	0.135
MSBP (mm Hg)	59.3 ± 12.6	58.2 ± 7.4	0.708
Inotrope score	14.7 ± 7.6	7.2 ± 2.8	0.001
Fluid resuscitation (mL/kg)	10.0 ± 6.6	3.0 ± 4.8	0.001
Base deficit	−1.3 ± 2.5	0.6 ± 2.4	0.019
Pao_2 (mm Hg)	46.5 ± 15.5	51.1 ± 22.1	0.466
Pao_2/Fio_2 ratio	56.0 ± 38.5	62.5 ± 35.2	0.572
Oxygenation index	16.7 ± 6.1	14.6 ± 5.6	0.304
$Paco_2$ (mm Hg)	42.4 ± 8.1	40.1 ± 6.56	0.304

[a] Mean ± standard deviation.

*i*NO = inhaled nitric oxide; MSBP = mean systemic blood pressure; n = total number of patients; $Paco_2$ = partial pressure of carbon dioxide; Pao_2 = partial pressure of oxygen; Pao_2/Fio_2 = partial pressure of oxygen to fraction of inspired oxygen ratio.

Table 3. Effect of i*NO Therapy on Glenn Pressures and Systemic Perfusion*

	Patients	0 Hour (Before *i*NO Therapy)[a]	1 Hour Post *i*NO Therapy[a]	3 Hours Post *i*NO Therapy[a]
Glenn pressure (mm Hg)	*i*NO responsive (n = 11)	22.7 ± 3.9	19.1 ± 3.4[b]	17.1 ± 3.4[c]
	*i*NO nonresponsive (n = 5)	21.6 ± 4.3	22.8 ± 4.6	23.2 ± 5.1
MSBP (mm Hg)	*i*NO responsive (n = 11)	57 ± 9.3	60.8 ± 7.8	60 ± 7.7
	*i*NO nonresponsive (n = 5)	64.4 ± 18.2	65.5 ± 16.3	63 ± 14.1
Inotrope score	*i*NO responsive (n = 11)	14.9 ± 8.7	11.8 ± 8.1[c]	11.4 ± 7.4[c]
	*i*NO nonresponsive (n = 5)	14.2 ± 6.4	14.2 ± 6.4	14.8 ± 7.2
Fluid volume support (mL/kg)	*i*NO responsive (n = 11)	11.4 ± 6.7	5.9 ± 4.4[b]	2.3 ± 3.4[c]
	*i*NO nonresponsive (n = 5)	7 ± 6.7	5 ± 7.1	5 ± 7.1
Base deficit	*i*NO responsive (n = 11)	−0.9 ± 2.0	1.09 ± 1.91[b]	1.1 ± 1.42[b]
	*i*NO nonresponsive (n = 5)	−1.9 ± 3.5	−0.04 ± 3.74	−0.26 ± 2.38

[a] Mean ± standard deviation. [b] p value < 0.05. [c] p value < 0.001.

*i*NO = inhaled nitric oxide; MSBP = mean systemic blood pressure.

hours, respectively, in 69% of patients after *i*NO initiation. In the remaining 31% of patients, an anatomic lesion explained the persistence of elevated Glenn pressures and decreased systemic perfusion.

Patients with elevated Glenn pressures had a statistically significant elevation of preoperative pulmonary artery pressures (17.5 ± 4.0 mm Hg) and pulmonary vascular resistance (2.6 ± 1.1 Woods units × meter^2) in our study. The reason for this elevation is unclear but it is well known that continuous release of endogenous nitric oxide from the pulmonary endothelium plays an important role in maintaining basal pulmonary vasorelaxation and low pulmonary artery pressures. Potentially, these patients could have poor baseline endogenous nitric oxide synthesis and/or release presenting as elevated baseline pulmonary vascular resistance. Furthermore, endothelial dysfunction after cardiopulmonary bypass [10] produces additional impairment of endogenous nitric oxide release. These two factors most likely contributed to the marked elevation of Glenn pressures observed. Response to *i*NO therapy in our study population is in contrast to previous studies that failed to show a beneficial effect of *i*NO in BDG patients [6, 8]. The postoperative Glenn pressures (17 ± 2 mm Hg and 17 ± 3 mm Hg) in their studies [6, 8] were lower than our patient population (22.4 ± 3.9 mm Hg). In our study, we failed to observe any further reduction in Glenn pressures 3 hours post-*i*NO therapy when pressures reached 17.1 ± 3.4 mm Hg. The *i*NO causes vasodilatation and reduction in pulmonary vascular resistance in the presence of pulmonary vasoconstriction. It has very little effect on pulmonary vascular resistance if the pulmonary vascular tone is not elevated [11] as observed in studies by Adatia and colleagues [6, 8].

Bidirectional Glenn shunt physiology requires a pressure gradient to be maintained between the superior vena cava and the pulmonary vasculature. It is, however, a low pressure circuit and any elevation of pulmonary artery resistance in BDG can be overcome by only marginal increases in superior vena caval pressure. A greater fluid volume and inotrope support was required initially in our patients to overcome the elevated Glenn pressures and to maintain systemic perfusion. The drop in Glenn pressures after *i*NO therapy facilitated forward flow from the superior vena cava to the pulmonary circulation, improving the stroke volume of the single ventricle and systemic perfusion, correlating with a significant reduction in inotrope score and fluid volume support.

Table 4. Effect of i*NO Therapy on Respiratory Indices*

	Patients	0 Hour (Before *i*NO Therapy)[a]	1 Hour Post-*i*NO Therapy[a]	3 Hours post-*i*NO Therapy[a]
Pao_2 (mm Hg)	*i*NO responsive (n = 11)	47.6 ± 16.3	51.9 ± 18.1	49.1 ± 8.9
	*i*NO nonresponsive (n = 5)	44 ± 14.1	44.4 ± 13.9	44.4 ± 6.2
Pao_2/FiO_2 ratio	*i*NO responsive (n = 11)	49.4 ± 17.3	57.5 ± 19.3[b]	74.3 ± 23.4[c]
	*i*NO nonresponsive (n = 5)	70.6 ± 66.4	57.8 ± 66.8	62 ± 35.9
Oxygenation index	*i*NO responsive (n = 11)	17 ± 5.2	12.9 ± 4.4[b]	12 ± 4.5[b]
	*i*NO nonresponsive (n = 5)	16 ± 8.5	18.4 ± 11.3	18.0 ± 7.7
$Paco_2$ (mm Hg)	*i*NO responsive (n = 11)	43.7 ± 6.6	38.9 ± 6.2[b]	41.4 ± 4.5
	*i*NO nonresponsive (n = 5)	39.6 ± 11	39.8 ± 8.5	38.6 ± 9

[a] Mean ± standard deviation. [b] p value < 0.05. [c] p value < 0.001.

*i*NO = inhaled nitric oxide; $Paco_2$ = partial pressure of carbon dioxide; Pao_2 = partial pressure of oxygen; Pao_2/FIo_2 = partial pressure of oxygen to fraction of inspired oxygen ratio.

Table 5. Failure of iNO Therapy

Patients	Cause of Failure	Second Operative Procedure	Outcome
Patient 1	Thrombus in right pulmonary artery	Surgical removal of thrombus	Survived
Patient 2	Glenn shunt stenosis	Redo of Glenn shunt	Survived
Patient 3	Narrow pulmonary arteries	Pulmonary arterioplasty	Survived
Patient 4	Patent BT shunt	Ligation of BT shunt	Survived
Patient 5	Aortopulmonary collaterals, poor ventricular function, left lung atelectasis	ECMO; BT shunt added	Died

BT shunt = Blalock-Taussig shunt; ECMO = extracorporeal membrane oxygenation; *i*NO = inhaled nitric oxide.

Serial evaluations of Pao_2/FIO_2 ratio and OI were incorporated in our study to assess pulmonary gas exchange. The Pao_2/FIO_2 ratio is a convenient and widely used index of oxygen gas exchange [12, 13]. Similarly, OI is an important index to monitor, serially, mechanical ventilation support and oxygenation as it takes PEEP, PIP, inspiratory time, and FIO_2 into consideration. The specific accuracy of pulmonary indices in patients with single ventricle physiology can be questioned. Although we believe that besides the absolute number the trends over time are an accurate indicator of an increase or loss in pulmonary function in these patients. Initially, the respiratory indices were potentially maintained by sustaining the pulmonary perfusion with increased inotrope and fluid volume support. After *i*NO therapy, although there seemed to be no significant difference in Pao_2, evaluation of respiratory indices revealed a significant improvement in the Pao_2/FIO_2 ratio and a reduction in OI at 1 and 3 hours post-*i*NO in the responsive patients. The *i*NO probably produced this improvement in pulmonary gas exchange not only by a reduction in Glenn pressures but also by amplifying the local alveolar hypoxic response [14], resulting in redistribution of blood flow to lung regions with a better ventilation to perfusion ratio [15]. The intrapulmonary distribution of blood flow and ventilation (V/Q distribution) that determines pulmonary gas exchange is commonly impaired after a cardiopulmonary bypass procedure [16]. The patient population in our study had a longer cardiopulmonary bypass time as compared with patients without elevated Glenn pressures, although it did not reach statistical significance ($p = 0.062$).

The *i*NO therapy did not cause sustained reduction in $Paco_2$ levels beyond 1 hour as appropriate ventilator changes were made to maintain $Paco_2$ levels in the normal range. The cerebral and pulmonary circulations are connected in series in BDG leading to direct competition of cerebral and pulmonary autoregulatory mechanisms. Hypercarbia has been demonstrated to improve cerebral blood flow, thereby increasing pulmonary blood flow and oxygenation after BDG in patients with normal Glenn pressures [17–19]. We maintained $Paco_2$ levels in the normal range as our patient population had markedly elevated Glenn pressures and hypercarbia is known to increase pulmonary vascular resistance.

Five patients in our study failed to show a significant response to *i*NO as demonstrated by no changes in Glenn pressures, inotrope score, fluid volume resuscitation, Pao_2/FIO_2 ratio, and OI. Anatomic lesions were found in all 5 patients, requiring a second operative procedure. A failure of significant response to *i*NO can be helpful to differentiate reversible elevated pulmonary vascular resistance from residual anatomic lesions [20].

Additionally, using logistic regression analysis our study demonstrates that all patients with preoperative pulmonary artery pressure 16 mm Hg or greater, followed by postoperative Glenn pressure 19 mm Hg or greater, required *i*NO in the immediate postoperative period. Several studies have identified preoperative pulmonary artery pressure less than 15 mm Hg as a desirable criterion to perform BDG [4, 21–24] and operations performed in patients with elevated pulmonary artery pressures have an increased risk of poor outcome [3, 25, 26].The *i*NO may be beneficial to manage BDG patients with elevated preoperative pulmonary artery pressures and pulmonary vascular resistance. Although our study had the limitations of no control group, cardiac output measurements, serum lactate levels, mixed venous oxygen saturations, or pulmonary function tests, we believe that a properly constructed randomized prospective study will be beneficial to validate our results.

We conclude that *i*NO therapy significantly reduces Glenn pressures and improves systemic perfusion and pulmonary gas exchange in a subset of patients with marked elevations in Glenn pressures after BDG. The *i*NO may have a therapeutic role in patients with elevated preoperative pulmonary artery pressures and pulmonary vascular resistance who undergo BDG. Patients who fail to respond to *i*NO should be evaluated for anatomic lesions.

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INVITED COMMENTARY

In this retrospective review, Agarwal and colleagues [1] evaluated the effects of inhaled nitric oxide (iNO) in bidirectional Glenn patients who had elevated Glenn pressures immediately postoperatively. The effects of iNO on Glenn pressures, systemic perfusion, and respiratory indices were assessed. The study demonstrated that in a majority of these patients iNO lowered superior vena cava pressures and improved systemic perfusion and gas exchange. In the subset of patients who did not benefit from iNO, anatomic obstruction or ventricular dysfunction was subsequently noted, and those patients underwent further operative interventions.

This study provides a basis for stepwise evaluation of postoperative Glenn patients with significantly elevated Glenn pressures and diminished clinical cardiac output. An early trial of iNO is warranted to determine whether hemodynamics are compromised due to elevated pulmonary vascular resistance (PVR). If the Glenn pressure does not fall to at least 17 mm Hg, then anatomic obstruction or ventricular dysfunction is likely, and an echocardiogram followed by cardiac catheterization is indicated. This series also suggests that there is a role for iNO in successfully getting patients with borderline preoperative pulmonary artery pressure and PVR through the immediate postoperative period after a Glenn procedure. Use of iNO empirically to come off cardiopulmonary bypass and in the early postoperative period may eliminate a detrimental period of low cardiac output for such patients, particularly for those who have long bypass times. Although not examined in this study, patients with elevated PVR preoperatively may benefit most by the complete avoidance of cardiopulmonary bypass during the Glenn procedure when possible.

These results are thought provoking, because prior similar work looking at iNO in postoperative Glenn patients has yielded equivocal findings. Notably in this study, all of the patients who had elevated Glenn pressures postoperatively had significantly higher pulmonary artery pressures and pulmonary vascular resistance at preoperative catheterization. The postoperative Glenn pressures in these patients were more elevated than those of the patients in prior study populations. There may be a subset of single ventricle patients with altered endogenous nitric oxide synthesis or metabolism. In such patients with longstanding elevations in PVR, with additional endothelial dysfunction secondary

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