SURGERY FOR CONGENITAL HEART DISEASE

EFFECTS OF OXYGEN, POSITIVE END-EXPIRATORY PRESSURE, AND CARBON DIOXIDE ON OXYGEN DELIVERY IN AN ANIMAL MODEL OF THE UNIVENTRICULAR HEART

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Objective: Respiratory manipulations are a mainstay of therapy for infants with a univentricular heart, but until recently little experimental information has been available to guide their use. We used an animal model of a univentricular heart to characterize the physiologic effects of a number of commonly used ventilatory treatments, including altering inspired oxygen tension, adding positive end-expiratory pressure, and adding supplemental carbon dioxide to the ventilator circuit. **Results:** Lowering inspired oxygen tension decreased the ratio of pulmonary to systemic flow. This ratio was 1.29 ± 0.08 at an inspired oxygen tension of 100%, 0.61 ± 0.09 at an inspired oxygen tension of 21%, and 0.42 ± 0.09 at an inspired oxygen tension of 15% ($p < 0.05$ compared with an inspired oxygen tension of 100% and a positive end-expiratory pressure of 0 cm H₂O). High-concentration supplemental carbon dioxide (carbon dioxide tension of 80 to 90 mm Hg) added to the ventilator circuit decreased inspired oxygen tension from 1.29 ± 0.11 to 0.42 ± 0.12 ($p < 0.05$ compared with baseline). A mixture of 95% oxygen and 5% carbon dioxide (carbon dioxide tension of 50 to 60 mm Hg) did not decrease the pulmonary/systemic flow ratio significantly. All three types of interventions influenced systemic oxygen delivery, which was a function of the pulmonary/systemic flow ratio. As the pulmonary/systemic flow ratio decreased from initially high levels (greater than 1), oxygen delivery first increased and reached an optimum at a flow ratio slightly less than 1. As the pulmonary/systemic flow ratio decreased further, below 0.7, oxygen delivery decreased. The ability of systemic arterial and venous oxygen saturations to predict the pulmonary/systemic flow ratio was examined. Venous oxygen saturation correlated well with both pulmonary/systemic flow ratio and systemic oxygen delivery, whereas arterial oxygen saturation did not accurately predict either pulmonary/systemic flow ratio or oxygen delivery. **Conclusion:** This model demonstrated the value of estimating the pulmonary/systemic flow ratio before initiating therapy. When the initial ratio was greater than about 0.7, interventions that decreased the ratio increased oxygen delivery and were beneficial. When the initial pulmonary/systemic flow ratio was below 0.7, interventions that decreased the ratio

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decreased oxygen delivery and were detrimental. We conclude by presenting a framework to guide therapy based on the combination of arterial and venous oxygen saturations and the estimate of the pulmonary/systemic flow ratio that they provide. (J Thorac Cardiovasc Surg 1996;112:644-54)

The univentricular heart complexes, including the hypoplastic left heart syndrome, are common congenital heart defects and are the most common cardiac cause of neonatal mortality in the first week of life.¹ Death from cardiac failure ensues in essentially all untreated infants.² Management options have been described that range from observation without intervention to surgical palliation with or without cardiac transplantation.^{3,4} Surgical palliation results in a univentricular outflow that is divided between the pulmonary and systemic circulations. Early survival after palliation appears to be crucially dependent on the balance of pulmonary and systemic flows (Qp/Qs) between these two circulations.⁵ Anatomic and physiologic situations that result in an equal distribution of cardiac output to the two circulations appear to meet with better clinical results.⁶ The balance of pulmonary and systemic flow (Qp/Qs) is delicate and easily perturbed, both by subtle physiologic alterations and by therapeutic maneuvers such as changing inspired oxygen tension (Fio₂) or adding an inotropic agent.⁷

Current knowledge regarding the control of the pulmonary and systemic circulations is largely empiric and derived from clinical experience. To more thoroughly characterize the effects of therapeutic maneuvers on these flows, we developed an animal model of the univentricular heart.⁸ This preparation was constructed without cardiopulmonary bypass: first an innominate-pulmonary artery shunt was placed, and then a nonrestrictive atrial septostomy was formed. The tricuspid valve was then rendered incompetent. Occluding the right ventricular outflow then functionally removed the right ventricle from the circulation.

For our first protocol using this new model, we examined the manner in which changing ventilatory mechanics can balance the Qp/Qs ratio. Although diligent manipulation of the respirator is a cornerstone of medical treatment of patients with a univentricular heart, there has previously been little experimental data to guide therapy.⁹ Changes made in inspired oxygen concentration, addition of supplemental carbon dioxide to the inspired gas mixture, and positive end-expiratory pressure (PEEP) can all have effects on pulmonary vascular resistance

and may therefore alter pulmonary flow and the Qp/Qs ratio.¹⁰ Our first series of experiments was an attempt to more accurately define the physiologic consequences of these interventions.

Methods

Animals. Neonatal pigs ($n = 6$), 1 to 2 weeks old and weighing 3.5 to 6.0 kg, were used. The initial hematocrit value in these animals was $26\% \pm 4.5\%$. Animals were examined during the operation to rule out a patent ductus arteriosus. All animals were cared for in accordance with the "Guide for the Care and Use of Laboratory Animals" prepared by the Institute of Laboratory Animal Resources and published by the National Institutes of Health (NIH Publication No. 86-23, revised 1985). Additionally, all aspects of animal care were in accordance with the standards of the Institutional Animal Care and Use Committee of the University of Louisville.

Procedure. Each piglet was anesthetized with ketamine (30 mg/kg intravenously) and acepromazine (2 mg/kg intravenously) and was intubated. The animals were ventilated on a VIP Bird pediatric ventilator (Bird Products Corp., Palm Springs, Calif.), with initial settings of Fio₂ 100% and PEEP 0 cm H₂O. The initial respiratory rate was set at 20 breaths/min, and tidal volume was set at 15 to 20 ml/kg. Rate and tidal volume were adjusted to keep carbon dioxide tension between 35 to 45 mm Hg. Anesthesia was maintained with pentobarbital (5 mg/kg per hour intravenously).

Both groins were dissected, and systemic arterial blood pressure was monitored with a 5F Mikro-Tip catheter (Millar Instruments, Inc., Houston, Tex.) placed into the descending thoracic aorta via the femoral artery. The other femoral artery was cannulated to obtain arterial blood gases. A fluid-filled catheter was placed into the midportion of the inferior vena cava via the femoral vein to monitor central venous pressure. The rate of intravenous fluid administration was adjusted to keep the central venous pressure between 7 and 10 mm Hg throughout the experiment.

With the animal in the supine position, a median sternotomy was performed. The pericardium was tacked up to form a well. Heparin (1000 units) was given intravenously, and a 6 mm reinforced polytetrafluoroethylene graft* was placed from the innominate artery to the common trunk of the pulmonary artery. This was anastomosed end to end to the innominate artery and end to side to the pulmonary artery.

After the graft was completed, transit time flow probes (Triton, Inc., San Diego, Calif.) were placed on the

*Gore-Tex vascular graft, registered trademark of W. L. Gore & Associates, Inc., Newark, Del.

Fig. 1. The completed animal model. Flow probes are depicted about the graft and the aorta. The tricuspid valvotomy and the atrial septal defect are not depicted.

proximal aorta, to measure left ventricular outflow, and around the innominate artery just proximal to the graft, to measure graft flow. A 5F Mikro-Tip catheter was passed from the infundibular portion of the right ventricle into the common trunk of the pulmonary artery to monitor pulmonary artery pressure.

A 4F Rashkind septostomy catheter (Bard Inc., Billerica, Mass.) was then passed transvenously via the remaining femoral vein to create an atrial septal defect. The tip of the catheter was guided manually across the interatrial septum into the left atrium. The catheter balloon was then inflated with 1.5 ml of saline solution and the catheter was pulled back into the right atrium, establishing a wide communication between the atria.

The Rashkind catheter was then advanced into the right ventricle. The balloon was inflated and the catheter was slowly withdrawn, thereby snaring the chordae tendineae of the tricuspid valve. By repeated tearing of the chordae tendineae, the tricuspid valve could be rendered incompetent.

Occluding the right ventricular outflow tract completed the univentricular circuit. All systemic venous return was routed across the atrial septal defect into the left atrium. Pulmonary flow was maintained by that portion of the left ventricular outflow that exited the innominate artery and traversed the polytetrafluoroethylene graft to the pulmonary artery. Right ventricular distention was prevented by having rendered the tricuspid valve incompetent. The completed operative preparation is depicted in Fig. 1.

All pressure measurements were displayed on a Hewlett-Packard monitor (Hewlett-Packard Company, Andover, Mass.) and simultaneously recorded on a Gould

recorder (model TA-11, Gould, Inc., Valley View, Ohio). Aortic and graft flows were also recorded on the Gould recorder. Arterial blood gases were measured on a blood and electrolyte analyzer (Stat 5, Nova Biomedical, Norwood, Mass.). Venous oxygen saturations (S_{vO_2}) were measured with an oximetric catheter (Opticath, Abbott Laboratories, North Chicago, Ill.) placed in the mid-abdominal inferior vena cava and were continuously recorded on an Abbott Laboratories recorder. This catheter was calibrated with venous blood samples withdrawn from the inferior vena cava and analyzed on the Nova blood gas analyzer.

Protocol. After completing the operative preparation, we examined the influence of F_{iO_2} , PEEP, and supplemental carbon dioxide added to the ventilatory circuit on the Q_p/Q_s ratio. The animal's chest was closed during all ventilator manipulations.

The first set of interventions examined the effects of F_{iO_2} . Holding PEEP constant at 0 cm H_2O , we set the F_{iO_2} at 100%, 75%, 50%, and 21%. By adding supplemental nitrogen to the ventilator circuit, we lowered the F_{iO_2} to 15%. In each animal we varied the order of interventions.

We examined the actions of PEEP at two levels of F_{iO_2} . In four piglets, with F_{iO_2} set at 100%, we varied PEEP to 0, 5, 10, and 15 cm H_2O . In a second set of four piglets, with F_{iO_2} set at 21%, PEEP was set at 0, 7.5, and 15 cm H_2O . Again, the order of interventions was varied among animals. Each animal's chest was closed during all ventilator manipulations.

In the final set of interventions, supplemental carbon dioxide was added to the breathing circuit. Measurements were first made at settings of F_{iO_2} 100% and PEEP 0 cm. Two concentrations of carbon dioxide were used. Ninety-five percent carbon dioxide (high concentration) was added into the circuit at a rate of 2 to 4 cubic feet per hour with F_{iO_2} 100% and PEEP 0 cm. This concentration and rate were used to obtain an arterial carbon dioxide tension (P_{aCO_2}) of 80 to 95 mm Hg (mean 87 ± 6 mm Hg) and a pH of 6.83 ± 0.12 . Respiratory rate and tidal volume were not altered during this intervention. A lower concentration of a mixture of 5% carbon dioxide and 21% oxygen, similar to that used clinically, was then added to the circuit and observations were repeated. The lower concentration of administered carbon dioxide resulted in a P_{aCO_2} of 50 to 60 mm Hg (mean = 56 ± 3 mm Hg) and a pH of 6.99 ± 0.11 .

Data analysis and statistics. Pulmonary and aortic flow were measured directly. Systemic flow was calculated as aortic flow minus pulmonary flow, as all pulmonary flow was derived from the innominate artery via the innominate artery-pulmonary artery graft. The Q_p/Q_s ratio was then determined by dividing pulmonary flow by systemic flow. Pulmonary vascular resistance was determined as $(MPA - CVP)/Q_p$, where MPA = mean pulmonary artery pressure, CVP = central venous pressure, and Q_p = pulmonary flow. Systemic vascular resistance was defined as $(MAP - CVP)/Q_s$, where MAP = mean arterial pressure, CVP = central venous pressure, and Q_s = systemic flow (calculated from directly measured values). Systemic arterial oxygen content was calculated as $(1.38 \times \text{hemoglobin/dl} \times \text{systemic arterial oxygen saturation}) + (0.0031 \times \text{partial pressure of arterial oxygen})$ and

Fig. 2. Relation of F_{iO_2} and the Qp/Qs ratio, systemic vascular and pulmonary vascular resistance (SVR and PVR), and oxygen delivery. *Upper panel:* As F_{iO_2} is decreased the Qp/Qs ratio decreases. *Middle panel:* Systemic vascular resistance is unchanged by changes in F_{iO_2} , while pulmonary vascular resistance increases when F_{iO_2} decreases to 50% or less. *Lower panel:* Oxygen delivery is maximal for F_{iO_2} 50%. This F_{iO_2} is associated with a Qp/Qs of 0.7. * $p < 0.05$ compared with baseline or maximal value in lower panel.

oxygen delivery was calculated as systemic arterial content $\times$ systemic arterial flow.

A one-way analysis of variance was used to analyze the relationship between F_{iO_2} and Qp/Qs, F_{iO_2} and pulmonary and systemic vascular resistance, and F_{iO_2} and oxy-

gen delivery. One-way analysis of variance was also used to analyze the relationship of PEEP and these variables. Linear regression analysis was used to determine the correlation between arterial oxygen saturation (SAO_2) and oxygen delivery and SvO_2 and oxygen delivery.

Fig. 3. Influence of the Qp/Qs ratio on oxygen delivery. Oxygen delivery is at a maximum for a Qp/Qs ratio of about 0.7, and it decreases when the Qp/Qs ratio either increases or decreases from this range. * $p < 0.05$ compared with maximal value for oxygen delivery.

Results

At baseline conditions of FiO₂ 100% and PEEP 0 cm H₂O, mean aortic flow in all animals was 1270 ± 118 ml/min, systemic flow was 569 ± 68 ml/min, and mean pulmonary (graft) flow was 700 ± 52 ml/min. Mean aortic pressure was 38 ± 4 mm Hg and mean pulmonary artery pressure was 21 ± 3 mm Hg. The Qp/Qs ratio for individual animals ranged from 0.94 to 1.71, with a mean of 1.29 ± 0.08 .

Effect of FiO₂. Fig. 2 shows the influence of FiO₂ on the Qp/Qs ratio, pulmonary and systemic vascular resistances, and oxygen availability. As seen in the *top panel*, as FiO₂ was lowered, the Qp/Qs ratio decreased, going from 1.29 ± 0.08 for FiO₂ 100% to 0.42 ± 0.09 for FiO₂ 15% ($p < 0.05$).

The decrease in the Qp/Qs ratio appeared to be related to the actions of lower FiO₂ on pulmonary vascular resistance. As seen in the *middle panel*, pulmonary vascular resistance increased at FiO₂

21% and 15%, going from a baseline of 131 ± 11 dyne · sec/cm at FiO₂ 100% to 412 ± 13 dyne · sec/cm at FiO₂ 15% ($p < 0.05$). Although systemic vascular resistance appeared to decrease somewhat as FiO₂ was lowered, these changes were not statistically significant.

By measuring Sao₂ and Svo₂, we were able to determine the influence of FiO₂ on systemic oxygen delivery. Oxygen delivery initially increased as FiO₂ was decreased, and then declined rapidly as FiO₂ was decreased further, with a significant difference between maximal oxygen delivery (seen with FiO₂ 50%) and the minimum (seen with FiO₂ 15%, $p < 0.05$).

Fig. 3 depicts the relationship of oxygen delivery to the Qp/Qs ratio. Oxygen delivery was at a maximum at a Qp/Qs ratio of approximately 0.7. Thus decreasing FiO₂ from 100% to 50%, by shifting the Qp/Qs ratio to 0.71, optimized oxygen delivery. As decreasing FiO₂ further lowered the Qp/Qs ratio below 0.7, oxygen delivery fell.

Fig. 4. Relation of SaO_2 and SvO_2 to the Qp/Qs ratio. *Upper panel:* SaO_2 increases as the Qp/Qs ratio increases, but it plateaus for higher values of Qp/Qs. *Lower panel:* SvO_2 increases as the Qp/Qs ratio increases, reaches a maximum at a Qp/Qs ratio slightly less than 1, and then decreases for higher Qp/Qs ratios.

Fig. 5. Relation of PEEP, the Qp/Qs ratio, and systemic vascular and pulmonary vascular resistance. *Upper panel:* The Qp/Qs ratio decreases as PEEP is increased. This effect adds to the effects of lower FiO₂. *Middle panel:* This effect is largely due to the increase seen in pulmonary vascular resistance. **p* < 0.05 compared with baseline (0 PEEP). *Lower panel:* Effect of PEEP on oxygen delivery is not constant.

We also examined the ability of SaO_2 and SvO_2 to predict the Qp/Qs ratio. Fig. 4 shows a plot of SaO_2 and SvO_2 versus a range of Qp/Qs ratios generated by varying FiO₂. Both SaO_2 and SvO_2

form curves, but SaO_2 plateaus for a Qp/Qs greater than 1, whereas SvO_2 declines for a Qp/Qs greater than 1. It can be seen that the curve for SvO_2 closely approximates that for oxygen delivery

(Fig. 3), with both curves having optimums at a Qp/Qs ratio of about 0.7.

Effects of PEEP. We examined the actions of PEEP at two different levels of Fio_2 —100% and 21%. Fig. 5 shows the effect of PEEP on the Qp/Qs ratio and pulmonary and systemic vascular resistances for the two groups. The *upper panel* demonstrates that at an Fio_2 of 100%, increasing PEEP lowered the Qp/Qs ratio. A similar trend was seen for an Fio_2 of 21%. Although the baseline Qp/Qs ratio was lower with an Fio_2 of 21%, addition of PEEP was able to lower the Qp/Qs ratio further, suggesting that the effects of PEEP and lowered Fio_2 are additive.

As was the case with Fio_2 , the decreases in the Qp/Qs ratio that came from increasing PEEP appeared to be related to increases in pulmonary vascular resistance. This is seen in the *middle panel* of Fig. 5, where an increase in PEEP from 0 to 15 cm H_2O led to an elevation in pulmonary vascular resistance from 118 ± 13 to 297 ± 17 dyne $\cdot$ sec/cm ($p < 0.05$).

The *lower panel* of Fig. 5 shows the effect of PEEP on oxygen delivery. As was the case with lowering Fio_2 , increasing PEEP initially increased and then decreased oxygen delivery.

Effect of supplemental carbon dioxide. Adding carbon dioxide to the ventilator circuit decreased the Qp/Qs ratio and increased pulmonary vascular resistance. High concentrations of supplemental carbon dioxide ($\text{Paco}_2 = 80$ to 95 mm Hg, mean $\text{pH} = 6.83 \pm 0.12$) decreased the Qp/Qs ratio from 1.33 ± 0.11 to 0.42 ± 0.12 when compared with a baseline of Fio_2 100% and PEEP 0 cm H_2O ($p < 0.05$). Pulmonary vascular resistance increased with carbon dioxide administration from 131 ± 11 to 432 ± 81 dyne $\cdot$ sec/cm ($p < 0.05$). The decrease in the Qp/Qs ratio affected oxygen delivery, decreasing it from 99 ± 15 to 68 ± 11 ml/min ($p < 0.05$).

Similar but greatly diminished effects were seen when concentrations of carbon dioxide similar to those used clinically were examined ($\text{Paco}_2 = 50$ to 60 mm Hg, mean $\text{pH} = 6.99 \pm 0.11$). These concentrations of carbon dioxide lowered the Qp/Qs ratio from 1.33 ± 11 to 1.25 ± 0.31 ($p = \text{NS}^*$), whereas pulmonary vascular resistance increased from 131 ± 21 to 145 ± 46 dyne $\cdot$ sec/cm ($p = \text{NS}$). The different results seen with high and low concentrations of carbon dioxide suggest that the effects of supplemental carbon dioxide are dose dependent.

*NS = Not significant.

Measurements of oxygen delivery. Fig. 6 contains individual data points from all experiments and interventions in this study. The *upper panel* shows the relationship of Sao_2 to oxygen delivery, and the *lower panel* plots the relationship of Svo_2 to oxygen delivery. Sao_2 appears to have a roughly linear relation to oxygen delivery at lower saturations but no correlation for higher saturations ($r = 0.26$, $p = \text{NS}$). The poor correlation between higher values of Sao_2 and oxygen delivery represents data taken at points with a Qp/Qs ratio greater than 1. At these values of Qp/Qs, oxygen delivery decreases as the Qp/Qs ratio increases, whereas Sao_2 remains elevated.

The *lower panel* of Fig. 6 demonstrates the correlation between oxygen delivery and Svo_2 , higher levels of Svo_2 being associated with higher oxygen delivery ($r = 0.81$, $p < 0.1$). These data suggest that Svo_2 provides a good estimate of oxygen delivery and that maximizing Svo_2 should maximize oxygen delivery.

Discussion

Background. Managing infants born with a univentricular heart is a complex and challenging task.¹¹ Although newer, aggressive surgical approaches now provide an alternative to the earlier policy of expectant management, overall survival is still limited.¹² The poor survival is at least partially caused by the marked hemodynamic instability that can characterize the clinical course of these infants. Improved medical management, then, should lead to better outcomes in this defect.

Although clinical experience has shown that controlling the relative amounts of pulmonary flow and systemic flow is an important determinant of outcome, the physiologic basis of interventions designed to alter these flows has not been fully characterized.¹³ We created an animal model of the univentricular heart in the hope that developing a better understanding of this physiology could provide the foundation for improved therapeutics.⁸

Our initial experiments focused on a number of respiratory interventions, inasmuch as these are a mainstay of present management techniques. We found that lowered Fio_2 decreased the Qp/Qs ratio, primarily by increasing pulmonary vascular resistance. Thus changing Fio_2 from 100% to 15% lowered the Qp/Qs ratio by 67% and increased pulmonary vascular resistance almost fourfold. PEEP had similar actions, with increased PEEP decreasing Qp/Qs ratio by 63% and increasing pul-

Fig. 6. Relation of SaO_2 and SvO_2 to oxygen delivery. *Upper panel:* SaO_2 becomes a poor predictor of oxygen for higher values of SaO_2 ($r = 0.26$). *Lower panel:* Good correlation between SaO_2 and oxygen delivery ($r = 0.82$).

monary vascular resistance almost threefold. The effects of lowering Fio_2 and PEEP were additive, because PEEP added to the ventilator circuit at an Fio_2 of 21% decreased the Qp/Qs ratio further and increased pulmonary vascular resistance. Adding carbon dioxide to the breathing circuit also decreased Qp/Qs and increased pulmonary vascular resistance. Different concentrations of carbon dioxide had different magnitudes of effects on the Qp/Qs ratio and pulmonary vascular resistance, suggesting that carbon dioxide could be “titrated” for a desired change in Qp/Qs.

Two other groups have used animal models of the univentricular circulation to examine the effects of ventilator changes, and their findings have been similar to ours. Mora and associates¹⁴ studied a porcine model, created with cardiopulmonary bypass and hypothermic circulatory arrest, which incorporated a central shunt between the innominate and pulmonary arteries. They found that pulmonary vascular resistance increased as the concentration of carbon dioxide increased. Although the effects of carbon dioxide on the Qp/Qs ratio were not measured directly, this study suggests that carbon dioxide can be used to balance the Qp/Qs ratio and that it can be “titrated” for dose-dependent effects. Reddy and colleagues¹⁵ used a model, constructed in fetal sheep, that was based on a Damus-Stansel-Kaye procedure. The effects of nitric oxide at 80 ppm, 100% Fio_2 , 10% Fio_2 , and 5% carbon dioxide on the Qp/Qs ratio were examined. As in our study, lower Fio_2 and supplemental carbon dioxide decreased the Qp/Qs ratio, whereas nitric oxide increased the Qp/Qs ratio.

The present study went beyond simply delineating the effects of certain respiratory interventions on the Qp/Qs ratio, however, and examined the effects of these interventions on oxygen delivery. An earlier, computer-generated analysis of the univentricular circulation, which we¹⁶ performed, suggested that a given intervention did not produce a constant change in oxygen delivery, but oxygen delivery was instead a function of the Qp/Qs ratio. This analysis suggested that the effects of therapeutics on oxygen delivery were determined by the Qp/Qs ratio at the time the manipulation was made.

This study confirmed the predictions of our theoretic analysis: although altering certain ventilator parameters could predictably change pulmonary vascular resistance and the Qp/Qs ratio, the resulting changes in oxygen delivery were not consistent. We found that if the initial Qp/Qs ratio was high, a

maneuver that lowered the ratio increased oxygen delivery, whereas for Qp/Qs ratios at or below 0.7, the same intervention decreased oxygen delivery (see *bottom panel* in Fig. 2 and in Fig. 3). These findings suggest that it may be necessary to obtain an estimate of the Qp/Qs ratio to predict the effect an intervention will have on oxygen delivery.

In the preoperative state, where Qp/Qs ratios up to 4 are seen, interventions that lower the ratio are almost uniformly beneficial. After first-stage palliation, however, Qp/Qs ratios are lower, ranging from 0.5 to 1.5,¹⁷ and it is in this situation that lowering the Qp/Qs ratio may be detrimental. Although obtaining an estimate of the initial Qp/Qs ratio could potentially improve therapeutic decision making, in clinical practice directly measuring the ratio is difficult. Our study demonstrates that Sao_2 and Svo_2 may be useful tools to estimate the Qp/Qs ratio.

As seen in Figs. 3 and 4, there is a good correlation between the Qp/Qs ratio and both oxygen delivery and Svo_2 . As the Qp/Qs ratio increased, both oxygen delivery and Svo_2 initially increased; both then decreased as Qp/Qs went past an optimum range. The correlation between Svo_2 and oxygen delivery implies that interventions that increase Svo_2 increase oxygen delivery, thereby leading to a more stable clinical situation.

Although Svo_2 is a useful predictor of oxygen delivery, it cannot yield a precise value for the Qp/Qs ratio. The reason is that the relation of Svo_2 to the Qp/Qs ratio is two-tailed, so that a low value for Svo_2 may represent either a very high or very low Qp/Qs ratio. Our data show that the addition of Sao_2 data to Svo_2 measurements can provide a better estimate of the ratio. Because Sao_2 remains high even for “excessive” Qp/Qs ratios, a combination of high Sao_2 and low Svo_2 represents a Qp/Qs ratio that is higher than optimal. Conversely, a low Svo_2 coupled with a low Sao_2 signifies a Qp/Qs ratio below optimum. When both Sao_2 and Svo_2 are high, a near optimal condition exists.

The Sao_2 data alone cannot be used to estimate the Qp/Qs ratio, because it reaches a plateau for values of the ratio greater than 1. Thus, Sao_2 fails to distinguish between a Qp/Qs ratio of 1 or a ratio of 3, even though one ratio is associated with clinical instability. This has been amply demonstrated in the clinical studies of Rossi and associates,¹⁸ who reported a number of instances in which children with adequate Sao_2 readings had profound clinical instability. Of note, in all of these cases clinical deterioration was preceded by a decline in Svo_2 .

With the use of the framework derived from our model, SaO_2 and SvO_2 measurements should be useful guides for therapy. Under this schema, when both SaO_2 and SvO_2 are high, an optimum exists and no further interventions are necessary. High values of SaO_2 and low values of SvO_2 , seen with excessive Qp/Qs ratios, indicate that oxygen delivery could be increased by lowering the ratio, either by decreasing F_{IO_2} , or by adding PEEP to the ventilator circuit. Conversely, if pulmonary venous oxygen saturations and cardiac output are adequate and both SaO_2 and SvO_2 are low, then the Qp/Qs ratio is too low, and lowering pulmonary vascular resistance, either by increasing F_{IO_2} or decreasing PEEP (if any is present in the ventilator circuit), would increase oxygen delivery.

Limitations of the study. The major limitation of this model is the limited range of Qp/Qs produced. Even with an F_{IO_2} of 100% the mean Qp/Qs ratio was only 1.29, and the highest individual animal Qp/Qs was 1.79. This limitation occurred despite the use of a 6 mm innominate–pulmonary artery graft. The lack of a large pressure gradient across the graft suggests that species differences in pulmonary vasculature, rather than technical difficulties in completing the model, led to a limited Qp/Qs ratio. This limited range of Qp/Qs precludes us from determining a value of F_{IO_2} that would result in an optimum Qp/Qs ratio in the human newborn infant. This limited range also likely explains why we found that oxygen delivery was maximal at an F_{IO_2} of 50%.

Despite these limitations, this study still allows valuable conclusions to be drawn regarding the effects of a number of respiratory interventions on oxygen delivery. It also demonstrates the usefulness of monitoring SaO_2 and SvO_2 to guide therapeutic choices and assess outcomes.

Conclusion

New animal models of univentricular heart defects have provided the potential to examine the effects of different management strategies in a systematic fashion. It is our hope that the creation of an armamentarium of therapeutics that can be administered with predictable consequences will lead to improved survival for infants born with these defects. We believe that our study demonstrates the need to examine all potential therapeutics in the context of their effects on oxygen delivery. We hope that the schema we presented for using SaO_2 and SvO_2 to estimate the Qp/Qs ratio will be a useful tool to choose therapies and assess their effectiveness.

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