The Effects of Carbon Dioxide on Oxygenation and Systemic, Cerebral, and Pulmonary Vascular Hemodynamics After the Bidirectional Superior Cavopulmonary Anastomosis

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OBJECTIVES
We investigated the effects of different CO2 tensions on oxygenation, pulmonary blood flow (Qp), cerebral blood flow, and systemic blood flow (Qs) after the bidirectional superior cavopulmonary anastomosis (BCPA).

BACKGROUND
Hypoxemia refractory to management of a high pulmonary vascular resistance index (PVRI) may complicate recovery from the BCPA.

METHODS
After BCPA, CO2 was added to the inspired gas of mechanically ventilated patients. The Qp, PVRI, and systemic vascular resistance index (SVRI) were calculated from oxygen consumption, intravascular pressures, and oxygen saturations. Cerebral blood flow was estimated by near infrared spectroscopy and transcranial Doppler.

RESULTS
In nine patients (median age 7.1, range 2 to 23 months), arterial oxygen tension increased significantly (p < 0.005) from 36 ± 6 mm Hg to 44 ± 6 to 50 ± 7 mm Hg at arterial carbon dioxide tensions (PaCO2) of 35, 45, and 55 mm Hg, respectively and decreased to 40 ± 8 mm Hg at PaCO2 40 mm Hg. At a PaCO2 of 55 and 45 compared with 35 mm Hg, Qp, cerebral blood flow, and Qs increased significantly, PVRI, Qp/Qs, and the ratio of Qp to inferior vena caval blood flow were unchanged, but SVRI decreased.

CONCLUSIONS
We have demonstrated that after the BCPA, systemic oxygenation, Qp, Qs, and cerebral blood flow increased and SVRI decreased at CO2 tensions of 45 and 55 mm Hg compared with 35 mm Hg. We suggest that hypoxemia after the BCPA is ameliorated by a higher PaCO2 and that low PaCO2 or alkalosis may be detrimental. Hypercarbic management strategies may allow earlier progression to the BCPA, which may contribute to reducing the interval morbidity in patients with a functional single ventricle. (J Am Coll Cardiol 2004;44:1501–9) © 2004 by the American College of Cardiology Foundation

The bidirectional superior cavopulmonary anastomosis (BCPA) increases effective pulmonary blood flow (Qp) without increasing ventricular volume in children with congenital heart disease and a single functional ventricle (1,2). The success of the BCPA is considered to be exquisitely dependant on an unobstructed, low-resistance pulmonary vascular bed, and preoperative evaluation focuses upon identifying adverse hemodynamic parameters (3). Nevertheless, despite preoperative scrutiny, hypoxemia after the BCPA may be profound and defy therapy. Hypoxemia in the early postoperative period is considered often to be consequent upon the transiently elevated pulmonary vascular resistance that occurs after cardiopulmonary bypass and may limit the age at which the BCPA can be performed safely (4,5). Paradoxically, postoperative hypoxemia is refractory to conventional treatments aimed at decreasing pulmonary vascular resistance, especially in young infants (5). Hyperventilation and inhaled nitric oxide have been shown to be ineffective and do not improve oxygenation in the absence of intrapulmonary shunt (6,7). Hypercapnia with acidosis increases cerebral blood flow and pulmonary vascular resistance in the normal circulation, after cardiopulmonary bypass and during anesthesia (8–10). The physiologic effects of varying CO2 and pH after the BCPA, when cerebral venous blood returns directly to the pulmonary artery without interposition of a subpulmonary ventricle, are defined less well. Although Bradley et al. have demonstrated that hypoventilation, without acidosis, increases systemic oxygenation, it remains incompletely understood whether hypercarbia increases cerebral blood flow selectively or globally augments cardiac output after BCPA (11). Therefore, we investigated the effects of a range of CO2 tensions on systemic oxygenation and cerebral blood flow, systemic blood flow (Qs), and Qp in the postoperative period.

METHODS
The study protocol was approved by the research and ethics review board at the Hospital for Sick Children. Informed and signed consent was obtained from the parents of all subjects. Patients scheduled for a BCPA were enrolled in the preoperative clinic.
We measured sequential changes in systemic oxygenation and cerebral blood flow, Qp, and Qs at arterial carbon dioxide tensions (PaCO2) of 35, 45, and 55 mm Hg and then, 40 mm Hg. In the operating room, a cuffed endotracheal tube was inserted. The intravascular monitoring lines were placed after induction of anesthesia (superior vena cava [SVC], jugular venous bulb [JVB], inferior vena cava [IVC], or femoral venous [FV]) and at completion of the surgical operation (common atrial or pulmonary venous). To cannulate the JVB, we used a single lumen 3-F catheter inserted retrogradely into the right internal jugular vein. Correct placement was verified by X-ray. After arrival on the critical care unit, initial ventilator settings were adjusted to a PaCO2 of 35 mm Hg, guided by end-tidal CO2 obtained by mass spectrometry. Throughout the study, the transesophageal temperature was maintained between 36°C to 37.5°C and the fraction of inspired oxygen at 0.3. The patients received infusions of propofol at 4 mg/kg/h, vecuronium by X-ray to exclude pleural effusions or parenchymal abnormalities. In five of nine patients, pulmonary venous oxygen saturations were assumed according to the method of

Table 1. Clinical and Operative Details

<table>
<thead>
<tr>
<th>Case</th>
<th>Age (months)</th>
<th>Weight (kg)</th>
<th>Diagnosis</th>
<th>Previous Surgery</th>
<th>Current Surgery</th>
<th>CPB Time (min)</th>
<th>Circulatory Arrest Time (min)</th>
<th>Aortic Cross Clamp Time (min)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>6</td>
<td>7.9</td>
<td>HLHS</td>
<td>Norwood I</td>
<td>BCPA</td>
<td>102</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>2</td>
<td>6.5</td>
<td>7.1</td>
<td>D-TGA, TA</td>
<td>None</td>
<td>BCPA</td>
<td>101</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>3</td>
<td>23</td>
<td>11.2</td>
<td>UAVSD, HLV</td>
<td>PA band</td>
<td>BCPA, DKS</td>
<td>90</td>
<td>24</td>
<td>58</td>
</tr>
<tr>
<td>4</td>
<td>2</td>
<td>4.5</td>
<td>HLHS</td>
<td>Norwood I</td>
<td>BCPA, TV repair</td>
<td>120</td>
<td>0</td>
<td>45</td>
</tr>
<tr>
<td>5</td>
<td>7</td>
<td>5.7</td>
<td>PA, IVS, HRV</td>
<td>B-T shunt</td>
<td>BCPA</td>
<td>57</td>
<td>0</td>
<td>17</td>
</tr>
<tr>
<td>6</td>
<td>8</td>
<td>7.2</td>
<td>Dextrocardia, DORV, D-TGA, MA, HRV</td>
<td>PA band</td>
<td>BCPA, DKS</td>
<td>82</td>
<td>20</td>
<td>56</td>
</tr>
<tr>
<td>7</td>
<td>10.5</td>
<td>7.4</td>
<td>DILV, D-TGA, CoA, LAVV stenosis, HRV</td>
<td>Norwood I</td>
<td>BCPA</td>
<td>116</td>
<td>0</td>
<td>29</td>
</tr>
<tr>
<td>8</td>
<td>5</td>
<td>6.5</td>
<td>DILV, L-TGA, AS, CoA, HRV</td>
<td>Norwood I</td>
<td>BCPA</td>
<td>56</td>
<td>0</td>
<td>14</td>
</tr>
<tr>
<td>9</td>
<td>8</td>
<td>7.2</td>
<td>DORV, PS, HRV, Bilateral SVC</td>
<td>None</td>
<td>Bilateral BCPA, atrial septectomy</td>
<td>98</td>
<td>0</td>
<td>54</td>
</tr>
</tbody>
</table>

AS = aortic stenosis; BCPA = bidirectional cavopulmonary anastomosis; B-T = Blalock-Taussig shunt; CoA = coarctation of aorta; CPB = cardiopulmonary bypass; DILV = double-inlet left ventricle; DKS = Damus-Kaye-Stansel; DORV = double-outlet right ventricle; D-TGA = dextro transposition of the great arteries; HLHS = hypoplastic left heart syndrome; HLV = hypoplastic left ventricle; HRV = hypoplastic right ventricle; IVS = intact ventricular septum; LAVV = left atrioventricular valve; L-TGA = levo transposition of the great arteries; MA = mitral atresia; PA = pulmonary atresia; PS = pulmonary stenosis; SVC = superior vena cava; TA = tricuspid atresia; TGA = transposition of great arteries; TV = tricuspid valve; UAVSD = unbalanced atrioventricular septal defect.
Table 2. Hemodynamic, Blood Gas Parameters, Oxygen Consumption, and Co-oximetry

<table>
<thead>
<tr>
<th>PaCO₂ 35</th>
<th>PaCO₂ 45</th>
<th>PaCO₂ 55</th>
<th>PaCO₂ 40</th>
</tr>
</thead>
<tbody>
<tr>
<td>HR (beats/min)</td>
<td>120 ± 9</td>
<td>116 ± 15 (p = 0.62)*</td>
<td>118 ± 19 (p = 0.85)†</td>
</tr>
<tr>
<td>MAP (mm Hg)</td>
<td>65 ± 9</td>
<td>62 ± 7 (p = 0.57)*</td>
<td>59 ± 7 (p = 0.27)‡</td>
</tr>
<tr>
<td>SVCp (mm Hg)</td>
<td>15 ± 2</td>
<td>16 ± 2 (p = 0.34)*</td>
<td>17 ± 2 (p = 0.99)†</td>
</tr>
<tr>
<td>CAp (mm Hg)</td>
<td>8 ± 2</td>
<td>8 ± 3</td>
<td>8 ± 3</td>
</tr>
<tr>
<td>pH</td>
<td>7.43 ± 0.05</td>
<td>7.34 ± 0.06 (p = 0.0003)§</td>
<td>7.28 ± 0.06 (p = 0.0003)§</td>
</tr>
<tr>
<td>PaCO₂ (mm Hg)</td>
<td>35 ± 1.0</td>
<td>45 ± 1.6 (p = 0.0003)§</td>
<td>55 ± 0.9 (p = 0.0003)§§</td>
</tr>
<tr>
<td>PaO₂ (mm Hg)</td>
<td>36 ± 6</td>
<td>44 ± 6 (p = 0.0003)§</td>
<td>50 ± 7 (p = 0.0015)§§</td>
</tr>
<tr>
<td>VO₂ (ml/min/m²)</td>
<td>143 ± 28</td>
<td>135 ± 26 (p = 0.012)*</td>
<td>129 ± 27 (p = 0.11)†</td>
</tr>
<tr>
<td>SaO₂ (%)</td>
<td>72 ± 7</td>
<td>77 ± 5 (p = 0.029)*§</td>
<td>80 ± 5 (p = 0.30)†</td>
</tr>
<tr>
<td>SVC O₂ Sat. (%)</td>
<td>37 ± 7</td>
<td>54 ± 8 (p = 0.0003)§</td>
<td>59 ± 9 (p = 0.34)*</td>
</tr>
<tr>
<td>JVB O₂ Sat. (%)</td>
<td>34 ± 7</td>
<td>56 ± 11 (p = 0.001)*§</td>
<td>59 ± 11 (p = 0.71)†</td>
</tr>
<tr>
<td>IVC/FV O₂ Sat. (%)</td>
<td>55 ± 9</td>
<td>66 ± 5 (p = 0.002)§§</td>
<td>67 ± 6 (p = 0.97)†</td>
</tr>
<tr>
<td>PV O₂ Sat. (%)</td>
<td>93 ± 10</td>
<td>93 ± 11 (p = 0.19)*</td>
<td>97 ± 5 (p = 0.98)†</td>
</tr>
</tbody>
</table>

Values expressed as mean ± SD. *Adjusted p value for difference between PaCO₂ 35 and 45 mm Hg. †Adjusted p value for difference between PaCO₂ 45 and 55 mm Hg. ‡Adjusted p value for difference between PaCO₂ 55 mm Hg and back to PaCO₂ 40 mm Hg. §Significant p value ≤ 0.05. ¶Assumed in five patients.

Statistics. The data, collected at four levels of PaCO₂ (35, 45, 55 mm Hg, and then 40 mm Hg) were analyzed by repeated measures analysis of variance for an effect over time. A quadratic effect was indicated by a statistically significant parameter estimate for the quadratic time sequence effect. The actual estimate for the inverted parabolas was negative, indicating a plateau or a return to baseline for the outcome. Pair-wise comparison was performed between the data at different levels of CO₂; the overall p value and the adjusted p value for multiple comparisons were calculated using the Tukey-Kramer adjustment. A p value of <0.05 was considered significant. We used the statistical software SAS version 8.2 (Cary, North Carolina). The results are expressed as mean ± standard deviation or medians with a range.

RESULTS

Between November 1, 2002, and June 1, 2003, we enrolled 11 patients and studied 9 patients. Two patients were excluded because of postoperative bleeding that persisted after the first hour. The median age was 7.1 months (range 2 to 23 months), and the median weight was 7.2 kg (range 4.5 to 11.2). Diagnostic and operative details are displayed in Table 1. The median duration of cardiopulmonary bypass

Table 3. Calculated Flows, Flow Ratios, and Resistances

<table>
<thead>
<tr>
<th>PaCO₂ 35</th>
<th>PaCO₂ 45</th>
<th>PaCO₂ 55</th>
<th>PaCO₂ 40</th>
</tr>
</thead>
<tbody>
<tr>
<td>Qp (l/min/m²)</td>
<td>1.4 ± 0.4</td>
<td>1.8 ± 0.5 (p = 0.01)*§</td>
<td>1.8 ± 0.4 (p = 0.85)†</td>
</tr>
<tr>
<td>Qivc (l/min/m²)</td>
<td>1.7 ± 0.6</td>
<td>4.3 ± 4 (p = 0.02)*§</td>
<td>3.1 ± 2.9 (p = 0.44)†</td>
</tr>
<tr>
<td>Qs (l/min/m²)</td>
<td>3.1 ± 0.6</td>
<td>6.0 ± 4.2 (p = 0.009)*§</td>
<td>4.9 ± 3.0 (p = 0.48)†</td>
</tr>
<tr>
<td>Qp/Qivc (l/min/m²)</td>
<td>0.9 ± 0.4</td>
<td>0.6 ± 0.4 (p = 0.14)*</td>
<td>0.8 ± 0.4 (p = 0.42)†</td>
</tr>
<tr>
<td>Qp/Qs (l/min/m²)</td>
<td>0.5 ± 0.1</td>
<td>0.3 ± 0.2 (p = 0.19)*</td>
<td>0.4 ± 0.1 (p = 0.44)†</td>
</tr>
<tr>
<td>PVRI (WU·m²)</td>
<td>6.0 ± 1.9</td>
<td>5.3 ± 2.4 (p = 0.67)*</td>
<td>5 ± 1.9 (p = 0.96)†</td>
</tr>
<tr>
<td>SVRI (WU·m²)</td>
<td>19 ± 3.1</td>
<td>11 ± 5.9 (p = 0.0003)§</td>
<td>12 ± 3.6 (p = 0.95)†</td>
</tr>
</tbody>
</table>

Values expressed as mean ± SD. *Adjusted p value for difference between PaCO₂ 35 and 45 mm Hg. †Adjusted p value for difference between PaCO₂ 45 and 55 mm Hg. ‡Adjusted p value for difference between PaCO₂ 55 mm Hg and back to PaCO₂ 40 mm Hg. §Significant p value ≤ 0.05.

PaCO₂ = partial pressure of carbon dioxide; PaO₂ = arterial oxygen tension; Qp = pulmonary blood flow; Qs = systemic blood flow; PVRI = pulmonary vascular resistance index; Qivc = inferior vena cava blood flow; Qp = pulmonary blood flow; Qs = systemic blood flow; SVRI = systemic vascular resistance index; WU = Wood Units.
was 98 min (range 56 to 120 min), and aortic cross clamp time was 29 min (range 14 to 58 min). Circulatory arrest was used in two patients. Nine patients received an infusion of milrinone (0.33 to 0.66 \( \mu \text{g/kg/min} \)), and two received dopamine 5 \( \mu \text{g/kg/min} \) postoperatively. Phenoxybenzamine (0.25 mg/kg) was administered to two patients at the start of cardiopulmonary bypass and in one patient continued postoperatively (2 mg/kg/day).

Jugular venous bulb catheters and pulmonary venous catheters either could not be inserted or were incorrectly positioned in four and five of the nine patients, respectively. The end of the FV line was situated in the IVC in five of

### Table 4. Cerebral Blood Flow Markers

<table>
<thead>
<tr>
<th>PaCO₂</th>
<th>Transcranial A-V O₂ difference</th>
<th>NIRS-TOI</th>
<th>TCD peak velocity (cm/s)</th>
<th>TCD mean velocity (cm/s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>35</td>
<td>35 ± 4</td>
<td>38 ± 10</td>
<td>90 ± 19</td>
<td>40 ± 17</td>
</tr>
<tr>
<td>45</td>
<td>23 ± 6 (p = 0.0003)*§</td>
<td>48 ± 3</td>
<td>107 ± 27 (p = 0.01)*§</td>
<td>52 ± 13 (p = 0.009)*§</td>
</tr>
<tr>
<td>55</td>
<td>21 ± 6 (p = 0.68)†</td>
<td>51 ± 9</td>
<td>114 ± 23 (p = 0.42)†</td>
<td>55 ± 11 (p = 0.83)†</td>
</tr>
<tr>
<td>40</td>
<td>32 ± 4 (p = 0.0003)‡§</td>
<td>36 ± 12 (p = 0.0003)‡§</td>
<td>88 ± 19 (p = 0.02)‡§</td>
<td>45 ± 22 (p = 0.34)‡§</td>
</tr>
</tbody>
</table>

Values expressed as mean ± SD. *Adjusted p value for difference between PaCO₂ 35 and 45 mm Hg; †Adjusted p value for difference between PaCO₂ 45 and 55 mm Hg; ‡Adjusted p value for difference between PaCO₂ 55 mm Hg and back to PaCO₂ 40 mm Hg. §Significant p value ≤ 0.05.

A-V O₂ = arterio-venous oxygen difference; NIRS = near infrared spectroscopy; PaCO₂ = arterial carbon dioxide tension; TCD = transcranial Doppler; TOI = tissue oxygenation index.

![Arterial pH](image1)

![Arterial PaCO₂ (mm Hg)](image2)

![Systemic Oxygen Saturation (%)](image3)

![Arterial PaO₂ (mm Hg)](image4)

**Figure 1.** Arterial pH, arterial carbon dioxide tension (PaCO₂), oxygen saturation (SaO₂), and PaO₂ at PaCO₂ 35, 45, 55, and 40 mm Hg. The lines represent individual patient values with the bold line indicating the mean value. *Adjusted p value for difference between PaCO₂ 35 and 45 mm Hg, †Adjusted p value for difference between PaCO₂ 45 and 55 mm Hg, ‡Adjusted p value for difference between PaCO₂ 55 and 40 mm Hg.
nine patients and in the common femoral vein in the remainder. In four patients, for technical reasons we were unable to collect IVC saturations and transcranial Doppler traces at a PaCO2 of 40 mm Hg. No patient experienced an adverse event as a result of the study procedure.

The results are summarized in Tables 2 to 4 and Figures 1 to 4.

We found that arterial oxygen tension (PaO2) increased significantly from 36 ± 6 to 44 ± 6 to 50 ± 7 mm Hg at PaCO2 of 35, 45, 55 mm Hg, respectively and decreased to 40 ± 8 mm Hg when PaCO2 returned towards baseline at 40 mm Hg. The systemic O2 saturation increased significantly from 72 ± 7% to 77 ± 5% at PaCO2 of 35 compared with 45; the increase was sustained at 80 ± 5% at a PaCO2 of 55 mm Hg and decreased to 74 ± 8% when PaCO2 returned towards baseline at 40 mm Hg. At a PaCO2 of 45 compared with 35 mm Hg, Qp and cardiac output (Qs) increased significantly (1.4 ± 0.4 to 1.8 ± 0.5 and 3.1 ± 0.6 to 6.0 ± 4.2 l/min/m²); increases were sustained at a PaCO2 of 55 mm Hg [(Qp) 1.8 ± 0.4 and (Qs) 4.9 ± 3.0 l/min/m²] and decreased to [(Qp) 1.5 ± 0.4 and (Qs) 2.7 ± 0.5 l/min/m²] at a PaCO2 of 40 mm Hg. Pulmonary vascular resistance was 6.0 ± 1.9 WU/m² and remained unchanged. At a PaCO2 of 45 compared with 35 mm Hg, systemic vascular resistance decreased from 19 ± 3.1 to 11 ± 5.9 Um², remained 12 ± 3.6 Um² at PaCO2 55 mm Hg, and increased 18 ± 2.2 Um² at a PaCO2 of 40 mm Hg. The ratio Qp/Qs and the ratio of Qp to inferior vena caval blood flow (Qp/Qivc) were unchanged. Cerebral blood flow increased at a PaCO2 of 45 and 55 mm Hg and decreased when PaCO2 returned to 40 mm Hg. Between a PaCO2 of 35 and 45 mm Hg, the SVC, JVB, and IVC/FV saturations increased significantly but did not increase further between a PaCO2 of 45 and 55 mm Hg and decreased significantly at a PaCO2 of 40 mm Hg. The lowest pH was 7.28 ± 0.06.

The median duration of study was 2.5 h (range of 1.5 to 3.25 h).

**DISCUSSION**

In this study, we demonstrated that increasing PaCO2 from 35 to 55 mm Hg with respiratory acidosis improved systemic oxygenation, Qs, cerebral blood flow, and Qp and decreased systemic vascular resistance without increasing pulmonary vascular resistance after a BCPA. These changes were marked when PaCO2 increased from 35 to 45 mm Hg. Increasing the PaCO2 from 45 to 55 mm Hg augmented PaO2 and maintained favorable pulmonary, systemic and cerebral blood flows without increasing pulmonary vascular resistance. Furthermore, decreasing PaCO2 from 55 to 40 mm Hg, by withdrawing exogenous carbon dioxide, caused the return of all parameters towards baseline. These results may have important implications in the management of the hypoxemic child after the BCPA, and a permissive hypercapnic strategy may improve the postoperative course, particularly in young infants. It is equally evident that a PaCO2 lower than 45 mm Hg has a deleterious effect on oxygenation and hemodynamics and may be counterproductive after the BCPA.

The determinants of systemic oxygenation after the BCPA are multifactorial and depend upon pulmonary and cerebral blood flow, cardiac output, as well as intrapulmonary shunting (4,11,15,19). A unique aspect of the physiology of Qp after BCPA is the interaction of two highly regulated vascular beds—the cerebral and the pulmonary, which have opposite responses to changes in carbon dioxide and acid base status (20–22). We found that by three
indirect methods of measurement (the JVB saturation, near infrared spectroscopy, and transcranial Doppler) the cerebral blood flow significantly increased between PaCO$_2$ of 35 and 45 mm Hg but did not increase further at a PaCO$_2$ of 55 mm Hg. An increase in cerebral blood flow and decrease in cerebral vascular resistance is a well-known response to increasing arterial CO$_2$ tension (20). However, although cerebral blood flow and Qp increased, so too did cardiac output. Therefore, there was no change in the ratio of Qp/Qs or Qp/Qivc, suggesting that the effect of CO$_2$ on oxygenation after the BCPA was not the result of selective cerebral vasodilation with increased flow distribution to the brain but rather, through an increase in total Qs and decrease in systemic vascular resistance index (SVRI). This caused both an increase in Qp as well as increased IVC saturations and improved systemic oxygenation. Others have documented that modestly elevating CO$_2$ increases cardiac output after cardiac surgery and during anesthesia (23,24), and at least one report suggests that despite an increase of 64% in cardiac output selective cerebral vasodilation does not occur (25). Our study concurs with the preliminary observations of Fogel et al. (26) that additional CO$_2$ after BCPA improves oxygenation. In contrast to Fogel et al. (26), we did not demonstrate redistribution of Qs to the brain, although it is unclear whether Fogel et al. (26) measured descending aorta flow velocities directly. However, Fogel et al. studied patients with BCPA remote from the perioperative period, which may account for the different findings (26).

There are inherent difficulties in the practical application of the Fick principle that may have influenced our results. We may have underestimated Qp, especially at PaCO$_2$ tensions of 35 and 40 mm Hg, as directly measured pulmonary venous oxygen saturations were lower than the

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**Figure 3.** Transcranial arterio-venous oxygen difference, near infrared spectroscopy (NIRS)-tissue oxygenation index, peak transcranial Doppler velocity, and mean transcranial Doppler velocity at CO$_2$ 35, 45, 55, and 40 mm Hg. The lines represent individual patient values, with the bold line indicating the mean value. Peak and mean transcranial Doppler measurements were not available at an arterial carbon dioxide tension (PaCO$_2$) of 40 mm Hg in four patients. *Adjusted p value for difference between PaCO$_2$ 35 and 45 mm Hg. †Adjusted p value for difference between PaCO$_2$ 45 and 55 mm Hg. ‡Adjusted p value for difference between PaCO$_2$ 55 and 40 mm Hg.
assumed value. In addition, the difficulties in obtaining a true mixed oxygen saturation from the IVC are well known (27). We attempted to overcome the vagaries of streaming in the IVC by obtaining oxygen saturations from below the renal veins. However, it remains possible that we have overestimated Qivc and that the improvement in systemic oxygenation at a higher PaCO2 may have reflected a more favorable distribution of flow to the brain with an increased ratio of superior vena caval blood flow to inferior vena caval blood flow (Qsvc:Qivc) as described in the theoretical model of Santamore et al. (19). There was a significant decrease in the IVC, SVC, JVB, and arterial oxygen saturation on return to 40 mm Hg, which again suggests global decrease in cardiac output on withdrawal of CO2, though the calculated Qs did not reach statistical significance, probably because of a small sample size owing to missing data at a PaCO2 of 40 mm Hg. Nevertheless, Qs demonstrated a significant trend with a quadratic effect correlating with the four different tensions of PaCO2 time measurements, whereas the ratio of Qp to Qs remained unchanged. The VO2 decreased with additional CO2 and complemented the improvement in oxygenation and Qs. To our knowledge, the measurement of VO2 by mass spectroscopy should not be confounded by the addition of CO2 to the inspired gas.

Elevating arterial CO2 and particularly decreasing pH have been shown to cause pulmonary vasoconstriction in animals, in humans, and after surgical correction of congenital heart disease using cardiopulmonary bypass (8,21,22). Calculated baseline pulmonary vascular resistance index (PVRI) was increased in our study but did not increase with the addition of CO2, suggesting that pulmonary vasoconstriction does not predicate Qp after the BCPA. This is supported by the observation that treatment aimed at pulmonary vasodilation such as hyperventilation with alkalaosis or inhaled nitric oxide, despite an increase in cyclic guanosine monophosphate, does not improve systemic oxygenation after the BCPA (6,7). This has potentially important implications in the management of hypoxemia after the BCPA and suggests that measures aimed at increasing cardiac output will influence systemic oxygenation and improve oxygen delivery to a greater degree than pulmonary vasodilators. Hypercapnia has been shown to increase cerebral, mesenteric, and skin blood flow and tissue oxygenation (28). Furthermore, permissive hypercapnia in the management of adult respiratory distress syndrome has been shown to be beneficial not only by reducing lung injury but also by improving systemic cardiac output and oxygen delivery (29–32).

Systemic oxygenation after the BCPA also depends on the degree of intrapulmonary shunt and subsequent decrease in pulmonary venous saturation. In our study, there was a tendency for pulmonary venous saturations to increase with increasing CO2. A reciprocal relationship between alveolar to arterial oxygen difference and CO2 has been described in the anesthetized, mechanically ventilated human (33).

Elevations in CO2 have been reported to increase heart rate, blood pressure, and cardiac contractility as a result of endogenous catecholamine release (34). However, in the current study we did not observe changes in heart rate or blood pressure, perhaps because the changes in CO2 were modest and contin-
ued anesthesia blunted catecholamine release. Thus, our findings may not be reproducible in the awake, spontaneously breathing patient or with CO₂ above 55 mm Hg. However, they concur with previous studies in the anesthetized, mechanically ventilated human (31,32).

Troublesome hypoxemia may occur particularly in young infants after BCPA (5,35), and thus the strategy of permissive hypercapnia may be most applicable in infants less than six months of age.

Conclusions. We have demonstrated that after the BCPA systemic oxygenation, Qp, Qs, and cerebral blood flow increased and SVRI decreased at CO₂ tensions of 45 and 55 mm Hg compared with 35 mm Hg. We suggest that hypoxemia after the BCPA is ameliorated by a higher PaCO₂ and that low PaCO₂ or alkalosis may be detrimental. Hypercarbic management strategies may allow earlier progression to the BCPA, which may contribute to reducing the interval morbidity in patients with a functional single ventricle.

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REFERENCES
APPENDIX
Formulas used to calculate flows and resistances (15,19):

\[
Q_s = \text{cardiac output} = (Q_p + Q_{ivc})
\]

\[
Q_p = \left[ \frac{O_2 \text{ consumption}}{[(PV \ O_2 \ \text{sat} - SVC \ O_2 \ \text{sat}) \cdot Hb \cdot 1.39 \cdot 10]} \right] / BSA
\]

(SVC sat = pulmonary arterial saturation in BCPA; pulmonary venous oxygen saturation [PV O_2 sat] assumed 0.99 in five of nine patients)

\[
Q_s = \left[ O_2 \text{ consumption} \cdot (PV \ O_2 \ \text{sat} - IVC \ O_2 \ \text{sat}) / [(PV \ O_2 \ \text{sat} - SVC \ O_2 \ \text{sat}) \cdot (SaO_2 - IVC \ O_2 \ \text{sat}) \cdot Hb \cdot 1.39 \cdot 10] \right] / BSA
\]

(FV O_2 saturation substituted for IVC O_2 saturation in four cases)

\[
Q_{ivc} = Q_s - Q_p
\]

\[
SVRI = \left( \frac{MAP - CAp}{Q_s} \right)
\]

\[
PVRI = \left( \frac{SVCp - CAp}{Q_p} \right)
\]

BSA = body surface area; CAp = common atrial pressure; Hb = hemoglobin; MAP = mean arterial pressure; O_2 sat = oxygen saturation; Q_{ivc} = calculated IVC flow; Q_p = calculated pulmonary blood flow; PVRI = pulmonary vascular resistance index; SaO_2 = systemic arterial oxygen saturation; sat = saturation; SVC = superior vena cava; SVCp = superior vena caval pressure; SVRI = systemic vascular resistance index.