Modeling of the Norwood circulation: effects of shunt size, vascular resistances, and heart rate

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Migliavacca, Francesco, Giancarlo Pennati, Gabriele Dubini, Roberto Fumero, Riccardo Pietrabissa, Gonzalo Urceal, Edward L. Bove, Tain-Yen Hsia, and Marc R. de Leval. Modeling of the Norwood circulation: effects of shunt size, vascular resistances, and heart rate. Am J Physiol Heart Circ Physiol 280: H2076–H2086, 2001.—Hypoplastic left heart syndrome is the most common lethal cardiac malformation of the newborn. Its treatment, apart from heart transplantation, is the Norwood operation. The initial procedure for this staged repair consists of constructing a circulation where a single outlet from the heart provides systemic perfusion and an interpositioning shunt contributes blood flow to the lungs. To better understand this unique physiology, a computational model of the Norwood circulation was constructed on the basis of compartmental analysis. Influences of shunt diameter, systemic and pulmonary vascular resistance, and heart rate on the cardiovascular dynamics and oxygenation were studied. Simulations showed that 1) larger shunts diverted an increased proportion of cardiac output to the lungs, away from systemic perfusion, resulting in poorer O2 delivery, 2) systemic vascular resistance exerted more effect on hemodynamics than pulmonary vascular resistance, 3) systemic arterial oxygenation was minimally influenced by heart rate changes, 4) there was a better correlation between venous O2 saturation and O2 delivery than between arterial O2 saturation and O2 delivery, and 5) a pulmonary-to-systemic blood flow ratio of 1 resulted in optimal O2 delivery in all physiological states and shunt sizes.

HYPOPLASTIC LEFT HEART SYNDROME is a lethal condition characterized by a hypoplasia of the left ventricle, the mitral valve, the aortic valve, and the ascending aorta. Preoperative survival relies on the patency of the ductus arteriosus to supply the systemic circulation. The initial operation (Norwood stage I, Fig. 1) consists in using the pulmonary valve and the main pulmonary artery as the systemic outflow and interposing a shunt between the innominate artery and the right pulmonary artery as a source of pulmonary blood flow (5, 11). Despite improved prognosis with the introduction and refinement of the palliative Norwood operation, immediate postoperative mortality remains at 20–30%, even in high-volume centers (4). During the second stage of the operation, the pulmonary flow from the shunt is replaced by a superior vena cava-to-pulmonary arterial anastomosis, and the final stage consists in connecting the inferior vena cava to the pulmonary artery (total cavopulmonary connection).

After the first-stage reconstruction, the systemic and pulmonary circulations are in parallel, and the right ventricle acts as the sole hydraulic power source. The distribution of the cardiac output between the systemic and the pulmonary circulations is governed in part by the interposition shunt. Various pharmacological and therapeutic interventions in the early postoperative period are aimed at maintaining this delicate balance between the two circulations (3, 11).

We have developed a lumped-parameter model of the Norwood circulation to study the cardiovascular effects of changes in geometry of the interposition shunt, systemic and pulmonary vascular resistance, and heart rate.

MATERIALS AND METHODS

Mathematical Model

A lumped-parameter model of the Norwood circulation was built following the methodology previously used to model the fetal (2, 12) and neonatal circulation (14, 15). The model is made of three subsystems: the hypoplastic heart, the systemic circulation, and the pulmonary circulation (Fig. 2).
Heart. Models for both atria (left (LA) and right (RA)) and the single ventricle (SV) are mathematically similar; differences are reflected by defining appropriate values of the various parameters within each model.

Pressure within any cardiac chamber ($P_{cc}$) varies throughout the cardiac cycle because of changes of volume within the chamber ($V_{cc}$) and contractile activity of the sarcomeres. Active (systolic) and passive (diastolic) properties of the myocardium account for the total chamber pressure ($P_{cc}$). This can be expressed mathematically as (27)

$$P_{cc} = P_{cc,active}(t, V_{cc}) + P_{cc,passive}(t, V_{cc})$$

where $P_{cc,active}$ and $P_{cc,passive}$ are the active and passive pressure terms, respectively.

Active and passive pressure-volume relationships are nonlinear (26), despite the usual practice of approximating the active curve as a straight line (28). The active relationship changes during systole as contractile activity of the cardiac chamber changes. Furthermore, the slope [i.e., the elastance ($E$)] of the active curve decreases with increasing volume. We mimicked this behavior as a time-varying elastance $E_{cc}[V_{cc}(t)]$ that depends also on chamber volume. This elastance, which accounts for the isometric pressure-volume function, was coupled with a constant viscous term, $R_{wall}$, that is related to the dissipative properties of the myocardium

$$P_{cc,active}(t) = E_{cc}(V_{cc}, t) \cdot (V_{cc}(t) - V_{acc}) + R_{wall,cc} \frac{dV_{cc}(t)}{dt}$$

where $V_{acc}$ is the unstressed volume of the cardiac chamber (i.e., the volume at zero pressure). The viscous term was considered only for the ventricle (1).

Elastance can be expressed as a product of a pulsatile activation time function [$A_{cc}(t)$] and a purely volume elastance term [$E_{cc}(V_{cc})$]

$$E_{cc}(V_{cc}, t) = A_{cc}(t) \cdot E_{cc}(V_{cc})$$

Ranging between 0 during the diastole and 1 at the end of systole as a squared sinusoidal function, $A_{cc}(t)$ describes the excitation-relaxation pattern of the myocardial sarcomeres (1, 28). The activation function has the same form for the single ventricle and the atria and RA but has different initiation ($\Delta T$) and temporal lapse (Fig. 2). The expression of $E_{cc}(V_{cc})$ depends on the pressure-volume relationship during systole of the cardiac chamber. For both atria, we assumed a linear pressure-volume function so that $E_{RA}(V_{RA})$ and

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**Fig. 1.** Anatomic sketch of the Norwood operation stage I. IA, innominate artery; LPA, left pulmonary artery; LCA, left carotid artery; RPA, right pulmonary artery; RSA, right subclavian artery; LSA, left subclavian artery; CCA, common carotid artery; neoaorta, reconstructed systemic outflow made of the pulmonary valve and the main pulmonary artery. Gray areas represent prosthetic patch and shunt.

**Fig. 2.** A: hydraulic network of the model with the systemic-to-pulmonary shunt represented. Arrows indicate the normal direction of flow. Values of the shunt parameters are evaluated from 3-dimensional mathematical models of the connection. $Q_P$ and $Q_S$, pulmonary and systemic blood flow; $CO$, cardiac output; ASD, atrial septal defect; DA, descending aorta; LA, left atrium; Neoao, aortic valve; PAB, pulmonary arterial bed; PVB, pulmonary venous bed; RA, right atrium; SAB, systemic arterial bed; SVB, systemic venous bed; SV, single ventricle; SLV, systemic large veins; Tric, tricuspid valve. See MATERIALS AND METHODS for description of electrical equivalents. B: activation ($A$) functions for LA, RA, and SV. $T_s$, cardiac cycle duration; $T_e$, duration of systole.
E'_{LV}^{\text{max}}(V_{LV}) \) are constant. For the single ventricle, a second-order polynomial function is adopted where the elastance decreases linearly with increasing volume

\[ E_{SV}^{\text{max}}(V_{SV}) = E_{SV}^{\text{max}} + E_{SV}^{\text{max}} \cdot (V_{SV} - V_{SV}^{\text{max}}) \]

At diastole, when the muscle fibers are relaxed, the single ventricle and the atria fill through an exponential pressure-volume function (25, 28), reflecting the nonlinear elasticity of the relaxed muscle and pericardium

\[ P_{cc, \text{passive}}(t) = P_{cc, \text{passive}}^0 \cdot (e^{K_{cc}(V_{cc}(t) - V_{cc,0})} - 1) \]

where \( P_{cc, \text{passive}}^0 \) and \( K_{cc} \) are constant parameters.

Atrophicventricular [tricuspid (Tric)] and ventriculoarterial [neoorta (Neoao)] valves were mimicked as a series of an ideal unidirectional valve and resistance. Flows through these valves were described by a nonlinear relationship between the pressure drop \( \Delta P(t) \) and the volume flow rate \( Q(t) \) across them

\[ \Delta P_{\text{valv}}(t) = K_{\text{valv}} \cdot Q(t)^2 \quad \text{valv = Tric, Neoao} \]

Finally, the nonrestrictive atrial septal defect (ASD) that allows flow from the left into the right atrium was simulated as a constant resistance \( R_{\text{ASD}} \).

Vascular system. The vascular circulation was divided into two subsystems connected by the systemic-to-pulmonary shunt. The systemic subsystem consists of four compartments: descending aorta, systemic arterial bed, systemic venous bed, and systemic large veins. The pulmonary subsystem consists of proximal pulmonary arteries, pulmonary arterial bed, and pulmonary venous bed.

Each compartment (depicted as a block in Fig. 2) in the model was assumed to have a constant compliance (C), where \( C = -\alpha \Delta V(t)/\Delta P(t) \), where \( P(t) \) is the instantaneous local pressure and \( V(t) \) is the instantaneous compartmental blood volume. Law of mass conservation was applied to each compartment and, with adoption of the above definition for C, can be expressed as

\[ \sum Q_{\text{in}}(t) - \sum Q_{\text{out}}(t) = C \cdot \frac{dP(t)}{dt} \]

where \( \Sigma Q_{\text{in}}(t) \) and \( \Sigma Q_{\text{out}}(t) \) indicate the respective sum of the instantaneous volumetric flow rates at the inlet and the outlet of the compartment, respectively.

The momentum conservation law for each interconnection (depicted as lines in Fig. 2) between two compartments can be expressed as

\[ \Delta P(t) = R \cdot \dot{Q}(t) + L \cdot \frac{d\dot{Q}(t)}{dt} \]

where \( \Delta P(t) \) is the instantaneous pressure difference applied to the line ends, \( \dot{Q}(t) \) is the instantaneous volumetric flow rate, \( R \) is the purely viscous resistance, and \( L \) is the inertance. Inertial effects were taken into consideration in the large arteries only.

For the interposition shunt, local fluid dynamics are important. Hence, a more comprehensive expression for the momentum conservation law is used

\[ \Delta P(t) = R \cdot \dot{Q}(t) + K \cdot \dot{Q}(t)^2 + L \cdot \frac{d\dot{Q}(t)}{dt} \]

where \( K \) is a constant. The term \( K \cdot \dot{Q}(t)^2 \) accounts for the nonlinear effects of convective energy loss due to flow separations, eddies, vortices, and turbulence associated with flow. Previously, we showed that inertial effects in the shunt are negligible (9). Inasmuch as shunt parameters \( R \) and \( K \) can be expressed also as functions of the shunt diameter \( D \) (9, 29), the previous equation can be rewritten as

\[ \Delta P(t) = \frac{k_1}{D^2} \dot{Q}(t) + \frac{k_2}{D^2} \dot{Q}(t)^2 \]

where \( k_1 \) and \( k_2 \) are proportionality constants, which can be derived experimentally or computationally; \( k_1 \) is dependent on shunt length and blood viscosity, and \( k_2 \) depends on local geometry (shunt angle of insertion, length, and subclavian and pulmonary arterial diameters). Figure 3 reports \( R \) and \( K \) as functions of \( D \) obtained by steady-state computational simulations. Best fitting of the computational data points generated \( k_1 \) of 960 mmHg·(l/min)^{-1}·mm^4 and \( k_2 \) of 960 and 5,200 mmHg·(l/min)^{-2}·mm^4 (9).

Combined with equations describing the heart system, applications of the mass and momentum conservation laws generated a set of nonlinear algebraic differential equations that was solved using a Runge-Kutta algorithm of the fourth order with an adaptive step.

Clinical Data

Cardiac catheterization and angiographic data of 28 Norwood patients were available for this study. Some of these
data were used as input parameters; other data were used for validation of the model (Table 1). Twenty patients received a 3.5-mm shunt; a 4-mm shunt was used in the remaining eight patients. Table 1 summarizes the anatomic and hemodynamic data.

**Parameter Values**

The parameter values of the shunt have been described above; those of the single ventricle (passive and active pressure relationships) were obtained from previous studies of univentricular circulation (14, 15, 20, 23). No data were available on the pressure-volume relationship of the atri or on the flow resistance across an atrioventricular valve or an ASD in neonatal univentricular heart. Those parameters were extracted from a published model of the fetal heart at full term (17) after appropriate rescaling (13). They are listed in Table 2. Heart rate (HR) and duration of the cardiac cycle (Tc = 1/HR) were derived from our previous data set. Duration of ventricular systole (Tsv = 0.16 + 0.37Tc) increases linearly with duration of the cycle (1), and duration (Tsv,LA = Tsv,RA = 0.37Tc) and time advance (∆Tc = 0.02Tc) of atrial systole were calculated as fractions of Tc (24).

The parameter values of the remaining compartments of the circulation were extrapolated from our previous data of Table 2. Values of the parameters describing the heart

<table>
<thead>
<tr>
<th>Parameter Values</th>
<th>Value</th>
<th>Units</th>
</tr>
</thead>
<tbody>
<tr>
<td>Single ventricle</td>
<td></td>
<td></td>
</tr>
<tr>
<td>E_{LSV}</td>
<td>8.5</td>
<td>mmHg/ml</td>
</tr>
<tr>
<td>E_{MV}</td>
<td>-0.042</td>
<td>mmHg/ml²</td>
</tr>
<tr>
<td>R_{M}</td>
<td>0.09</td>
<td>mmHg·l⁻¹·min⁻¹</td>
</tr>
<tr>
<td>P_{c,SV}</td>
<td>0.9</td>
<td>mmHg</td>
</tr>
<tr>
<td>K_{c,SV}</td>
<td>0.062</td>
<td>ml⁻¹</td>
</tr>
<tr>
<td>V_{c,SV}</td>
<td>4.0</td>
<td>ml</td>
</tr>
<tr>
<td>Right atrium</td>
<td></td>
<td></td>
</tr>
<tr>
<td>E_{RA}</td>
<td>7.35</td>
<td>mmHg/ml</td>
</tr>
<tr>
<td>P_{c,RA}</td>
<td>0.17</td>
<td>mmHg</td>
</tr>
<tr>
<td>K_{c,RA}</td>
<td>0.484</td>
<td>ml⁻¹</td>
</tr>
<tr>
<td>V_{c,RA}</td>
<td>1.0</td>
<td>ml</td>
</tr>
<tr>
<td>Left atrium</td>
<td></td>
<td></td>
</tr>
<tr>
<td>E_{LA}</td>
<td>7.35</td>
<td>mmHg/ml</td>
</tr>
<tr>
<td>P_{c,LA}</td>
<td>0.17</td>
<td>mmHg</td>
</tr>
<tr>
<td>K_{c,LA}</td>
<td>0.484</td>
<td>ml⁻¹</td>
</tr>
<tr>
<td>V_{c,LA}</td>
<td>1.0</td>
<td>ml</td>
</tr>
<tr>
<td>ASD</td>
<td></td>
<td></td>
</tr>
<tr>
<td>R_{ASD}</td>
<td>0.001</td>
<td>mmHg·l⁻¹·min⁻¹²</td>
</tr>
<tr>
<td>Tricuspid valve</td>
<td></td>
<td></td>
</tr>
<tr>
<td>K_{Tric}</td>
<td>0.0004</td>
<td>mmHg·l⁻²·min⁻¹²</td>
</tr>
<tr>
<td>Neoaoorta</td>
<td></td>
<td></td>
</tr>
<tr>
<td>K_{neoao}</td>
<td>0.0004</td>
<td>mmHg·l⁻²·min⁻¹²</td>
</tr>
</tbody>
</table>

E, elastance; SV, single ventricle; R, resistance; P, pressure; K, constant; V, volume; u, unstressed; LA, left atrium; RA, right atrium; ASD, atrial septal defect; Tric, tricuspid; Neoao, neoaoorta.

**O₂ Calculations**

The O₂ transport model had the following unknown variables: O₂ contents (ml/dl blood) of the systemic arteries (C_{art}), of the systemic veins (C_{ven}), and of the pulmonary veins (C_{pv}). Because of the systemic-to-pulmonary shunt, O₂ content in the pulmonary arteries was equal to C_{art}. The first two governing equations were

\[ Q_S \cdot C_{ven} + Q_F \cdot C_{pv} = CO \cdot C_{art} \]

\[ Q_S \cdot (C_{art} - C_{ven}) = C_{o2} \]

where \( Q_F \) and \( Q_S \) are pulmonary and systemic mean blood volumetric flow rates, respectively, CO is cardiac output (CO = Q_P + Q_S), and \( C_{o2} \) is the whole body O₂ consumption. Volumetric flow rates were obtained from the lumped-parameter model of the newborn circulation.

A third equation was derived from the lung O₂ exchange model, based on the work by Hill et al. (7). This represented the effects of the capillaries in the pulmonary bed as a single unit with volume (V_{cap}) of 3.5 ml. Hence, variation of the partial pressure of O₂ (P_{o2}) with distance along the capillary bed was equivalent to the change of P_{o2} in an element of blood moving with time

\[
\frac{dP_{o2}}{dt} = D_m \cdot (P_{o2} - P_{o2}) / (\alpha + O_2 Cap \cdot \text{slope})
\]

Table 1. Clinical data obtained from catheterization exam

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Mean ± SD</th>
<th>Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, mo</td>
<td>5.07 ± 1.20</td>
<td>3.5–9</td>
</tr>
<tr>
<td>Weight, kg</td>
<td>6.51 ± 1.05</td>
<td>4.35–8.6</td>
</tr>
<tr>
<td>BSA, m²</td>
<td>0.33 ± 0.04</td>
<td>0.25–0.4</td>
</tr>
<tr>
<td>HR, beats/min</td>
<td>125.6 ± 16.35</td>
<td>88–156</td>
</tr>
<tr>
<td>Hb, g/dl</td>
<td>16.5 ± 1.96</td>
<td>11.8–20.8</td>
</tr>
<tr>
<td>CVO₂, ml·min⁻¹·m⁻²</td>
<td>156.2 ± 23.5</td>
<td>114–212</td>
</tr>
<tr>
<td>PVR, mmHg·m⁻²·min⁻¹</td>
<td>2.3 ± 0.7</td>
<td>0.8–3.7</td>
</tr>
<tr>
<td>SVR, mmHg·m⁻¹·min⁻¹</td>
<td>21.6 ± 5.3</td>
<td>11–36.4</td>
</tr>
<tr>
<td>PVR, mmHg·l⁻¹·min⁻¹</td>
<td>7.1 ± 2.5</td>
<td>2.4–13.1</td>
</tr>
<tr>
<td>SVR, mmHg·l⁻¹·min⁻¹</td>
<td>66.4 ± 17.5</td>
<td>30.6–113.8</td>
</tr>
<tr>
<td>Satarter, %</td>
<td>72.8 ± 5.4</td>
<td>61–80</td>
</tr>
<tr>
<td>Satventer, %</td>
<td>48.1 ± 5.6</td>
<td>36–56</td>
</tr>
<tr>
<td>Satarter, %</td>
<td>95.9 ± 3.11</td>
<td>87–100</td>
</tr>
<tr>
<td>Qp, l·min⁻¹·m⁻²</td>
<td>3.27 ± 1.04</td>
<td>1.6–6.4</td>
</tr>
<tr>
<td>Qs, l·min⁻¹·m⁻²</td>
<td>2.91 ± 0.70</td>
<td>1.6–4.6</td>
</tr>
<tr>
<td>Qp, l/min</td>
<td>1.07 ± 0.37</td>
<td>0.51–2.11</td>
</tr>
<tr>
<td>Qs, l/min</td>
<td>0.96 ± 0.27</td>
<td>0.51–1.60</td>
</tr>
<tr>
<td>Qp/Qs</td>
<td>1.17 ± 0.40</td>
<td>0.46–2.37</td>
</tr>
<tr>
<td>CO, l/min</td>
<td>2.04 ± 0.53</td>
<td>1.02–3.19</td>
</tr>
<tr>
<td>CO, l·min⁻¹·m⁻²</td>
<td>6.18 ± 1.33</td>
<td>3.20–9.10</td>
</tr>
<tr>
<td>CO, l·min⁻¹·kg⁻¹</td>
<td>0.41 ± 0.13</td>
<td>0.20–0.66</td>
</tr>
<tr>
<td>PAP, mmHg</td>
<td>13 ± 3</td>
<td>8–18</td>
</tr>
<tr>
<td>SBP, mmHg</td>
<td>104 ± 14</td>
<td>75–143</td>
</tr>
<tr>
<td>Systolic</td>
<td>45 ± 6</td>
<td>30–57</td>
</tr>
<tr>
<td>Diastolic</td>
<td>67 ± 10</td>
<td>48–95</td>
</tr>
<tr>
<td>Mean</td>
<td>7.14 ± 1.9</td>
<td>4–11</td>
</tr>
<tr>
<td>SVEF, %</td>
<td>54 ± 11</td>
<td>31–68</td>
</tr>
<tr>
<td>O₂ delivery, ml/min</td>
<td>156.8 ± 45.41</td>
<td>80.3–275.5</td>
</tr>
<tr>
<td>O₂ delivery, ml·min⁻¹·m⁻²</td>
<td>474.1 ± 110.3</td>
<td>251.0–736.9</td>
</tr>
</tbody>
</table>

BSA, body surface area; HR, heart rate; CVO₂, O₂ consumption; Satarter, arterial saturation; Satventer, venous saturation; Qp, pulmonary flow; Qs, systemic flow; CO, cardiac output; CI, cardiac index; PAP, mean pulmonary arterial pressure; PV, pulmonary vein; PVR, pulmonary vascular resistance; SVR, systemic vascular resistance; PVR, PVR-BSA (indexed PVR); SVR, SVR-BSA (indexed SVR); SBP, systemic blood pressure; SVEF, single ventricle ejection-diastolic pressure; O₂, single ventricle ejection fraction. *Input quantities for the mathematical model.
The following assumptions, based on clinical observations (Table 1), are made in the O2 calculations: Hb = 16.52 g/dl and CVO2 = 159.64 ml/min⁻¹·m⁻².

RESULTS

The mathematical model generated flow and pressure temporal tracings, as well as mean values of saturations and O2 delivery.

Validity of the Model

The mathematical model was validated by comparing the results of simulations with a part of the averaged (Table 1) and individual clinical data. The clinical parameters averaged from 28 patients, used as input of the model, were as follows: HR = 125.6 beats/min, indexed PVR (PVRs) = 2.3 mmHg·m⁻²·l⁻¹·min⁻¹, indexed SVR (SVRs) = 21.6 mmHg·m⁻²·l⁻¹·min⁻¹, and D = 3.5 mm. With those input parameters, the simulation showed a CO of 2.22 l/min with a cardiac index (CI) of 6.73 l·min⁻¹·m⁻², Qp/Qs of 1.14, pulmonary flow of 1.18 l/min, and mean systemic and pulmonary arterial pressures of 69 and 12 mmHg, respectively. Calculated O2 delivery was 546.9 ml·min⁻¹·m⁻², and arterial and venous O2 saturations were 79% and 55.9%, respectively.

Ventricular pressure-volume loops, temporal relationships of ventricular, aortic, and pulmonary arterial pressures, and flow in shunt and aorta are depicted on Fig. 4. The end-diastolic and systolic volumes were 34.9 and 16.9 cm³, respectively, with an ejection fraction of 51.6%.

There was a good correlation between the simulation and the averaged clinical data (Table 1) as well as published data (20, 23).

If one takes individual cases, however, whereas good correlations were obtained in some, there were discrepancies among others. Table 4 shows the ranges of predicted values for various parameters and the percent differences from the observed data. For these simulations, the measured pulmonary venous saturation for each patient was used.

Effects of Shunt Size

With the use of D as the independent variable, shunt hemodynamics were simulated for diameters of 3, 3.5, 4, 4.5, and 5 mm. Figure 5A demonstrates the result of the simulations where CI and Qp/Qs are reported as functions of shunt diameter. Enlarging the shunt diameter was associated with increases in CI and Qp/Qs, resulting in higher pulmonary flow. Augmentation in CI led to increased arterial O2 saturation (Fig. 5B), but not venous O2 saturation. On the other hand, O2 delivery (Fig. 5C) slightly increased when shunt diameter increased from 3 to 3.5 mm and sharply decreased for larger shunts as more blood is diverted to the pulmonary circulation at the expense of the systemic output. Effects of shunt size on mean pulmonary arterial pressure were nearly linear, inasmuch as varying the shunt size from 3 to 5 mm resulted in a pressure increase from 9 to 18 mmHg. Conversely, mean syst-
temic arterial pressure decreased from 81 to 59 mmHg. As expected, the pressure gradient along the shunt decreased as shunt diameter was enlarged, ranging from 72 to 41 mmHg for shunt diameter of 3–5 mm.

Effects of Vascular Resistances

Figure 6 shows CI, \( \dot{Q}_P/\dot{Q}_S \), arterial and venous saturations, and \( O_2 \) delivery as functions of PVRa (0.5–20 mmHg \( \cdot \) m\(^{-2}\) \( \cdot \) l\(^{-1}\) \( \cdot \) min) for shunt diameter of 3.5 mm and SVRa of 21.6 mmHg \( \cdot \) m\(^{-2}\) \( \cdot \) l\(^{-1}\) \( \cdot \) min. CI slightly decreased (from 7.0 to 5.9 l\(^{-1}\) \( \cdot \) min\(^{-1}\) \( \cdot \) m\(^{-2}\)), while \( \dot{Q}_P/\dot{Q}_S \) diminished from 1.23 to 0.64 (Fig. 6A). Arterial and venous saturations showed a similar decline (Fig. 6B), but \( O_2 \) delivery reached a maximum at PVRa of ~4–5 mmHg \( \cdot \) m\(^{-2}\) \( \cdot \) l\(^{-1}\) \( \cdot \) min (Fig. 6C). Mean systemic arterial pressure remained nearly constant (73–79 mmHg), while mean pulmonary arterial pressure showed abrupt elevation with higher PVRa (from 5.5 to 48 mmHg).

Effects of HR

Figure 8 illustrates the effects of increasing HR on CI, \( \dot{Q}_P/\dot{Q}_S \), arterial and venous \( O_2 \) saturations, and \( O_2 \) delivery. CI increased with HR, while \( \dot{Q}_P/\dot{Q}_S \) remained relatively unchanged (Fig. 8A). Arterial and venous \( O_2 \) saturations increased with respect to HR (Fig. 8B). An increase in HR from 60 to 180 beats/min produced an increase in \( O_2 \) delivery from 380 to 650 ml \( O_2 \) \( \cdot \) min\(^{-1}\) \( \cdot \) m\(^{-2}\) (Fig. 8C).

Elevated pressure gradients along the shunt were also observed with higher HR, ranging from 45 to 70 mmHg.

Simulation of Early Postoperative Period

In the early postoperative period, PVRa and HR are often increased by inotropic drugs. To evaluate this condition, simulations with PVRa twice the baseline value (4.6 mmHg \( \cdot \) m\(^{-2}\) \( \cdot \) l\(^{-1}\) \( \cdot \) min) and HR of 150 beats/
min were performed with various shunt diameters (3–5 mm). CI and $Q_{p}/Q_{s}$ were lower than the baseline values ($PVR_a = 2.3$ mmHg·m$^{-2}$·l$^{-1}$·min and HR = 120 beats/min at rest). This difference was accentuated for larger shunts (Fig. 9, A and B). $O_2$ balance remained almost unchanged (Fig. 9C).

**Simulation of Exercise**

Dynamic exercise is characterized by a marked increase in $O_2$ consumption, reduction in SVR$_a$, and elevation in HR (5, 6). We simulated this condition by increasing HR to 180 beats/min, reducing SVR$_a$ by 10.220.33.4 on April 19, 2017 http://ajpheart.physiology.org/ Downloaded from

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**Fig. 5.** Effects of shunt diameter on cardiac index (CI; A) and pulmonary-to-systemic flow ratio ($Q_{p}/Q_{s}$), arterial and venous saturations (Sat$_{art}$ and Sat$_{ven}$) (B), and $O_2$ delivery (C). PVR$_a$ and SVR$_a$ = 2.3 and 21.6 mmHg·m$^{-2}$·l$^{-1}$·min, HR = 120 beats/min. Shunt size is associated with increases in CI and $Q_{p}/Q_{s}$, resulting in higher pulmonary flow. Augmentation in CI led to an increase in arterial, but not venous, $O_2$ saturation.

**Fig. 6.** Effects of PVR$_a$ on CI and $Q_{p}/Q_{s}$ (A), changes in saturations (B), and $O_2$ delivery (C). Shaded areas represent the range of values of our patient population. SVR$_a$ = 21.6 mmHg·m$^{-2}$·l$^{-1}$·min, HR = 120 beats/min, shunt diameter = 3.5 mm. CI slightly decreases, while $Q_{p}/Q_{s}$ decreases. Arterial and venous saturations show a similar decline, but $O_2$ delivery reaches a maximum at PVR$_a$ = 4–5 mmHg·m$^{-2}$·l$^{-1}$·min.
exercise was always lower, despite use of larger shunts. Nevertheless, O₂ balance during exercise remained >1.5 and increased with larger shunts. It is possible that a combination of highly intensive exercise (i.e., higher CVO₂) and small shunts (3 or 3.5 mm) could lead to O₂ deficit.

Figure 9 demonstrates that when O₂ balance was plotted against Qp/Qs, the maximum level was reached at Qp/Qs ~ 1 for all three simulated physiological conditions. Similarly, O₂ delivery was at a maximum at
\[ \frac{Q_P}{Q_S} = 1 \] in all ranges of PVRa (Fig. 6) and shunt sizes (Fig. 5) simulated in our study.

**DISCUSSION**

This study confirms the clinical experience that the shunt is crucial in the regulation of pulmonary and systemic blood flow and, consequently, of tissue oxygenation.

Shunts of 3.5 mm diameter are most commonly used in neonates. Simulations of the early postoperative state confirm that a 3.5-mm shunt allows for a flow distribution between the systemic and the pulmonary circulations that provides a maximum level of \( O_2 \) delivery. In the simulation of exercise, however, a 3.5-mm shunt did not provide enough \( O_2 \) to achieve an optimal \( O_2 \) balance. Whereas larger shunts would meet these increased \( O_2 \) requirements during exercise, they would result in a reduction of \( O_2 \) delivery at rest because of excessive pulmonary flow and reduced systemic flow.

Inasmuch as demand on shunt performance varies with changes in physiological conditions, one limitation of the Norwood operation is the inability of the shunt to satisfy all these conditions. Similarly, the nature of the shunt does not provide for adjustments for growth.

The optimal \( O_2 \) delivery is achieved when balanced pulmonary and systemic perfusion is established, namely, when \( \frac{Q_P}{Q_S} \sim 1 \). This is true regardless of shunt size, physiological state, or absolute values of PVR. In other words, when pulmonary and systemic perfusions are equal, the Norwood circulation is optimized.

In practice, despite the fixed nature of the shunt, when \( O_2 \) requirements change, manipulation of the PVR and SVR is used to maintain the optimal flow ratio. This was confirmed by the introduction in the lumped-parameter model of changes in SVR and PVR similar to those produced by therapeutic manipulation, such as changes in inspired \( P_{O_2} \), positive end-expiratory pressure, nitric oxide inhalation, and supplemental \( CO_2 \) (10, 16–18).

The importance of monitoring venous \( O_2 \) saturation as an indicator of tissue \( O_2 \) delivery in the postoperative period has been previously reported (19) and confirmed by our simulations. In all situations, there was a better correlation between venous \( O_2 \) saturations and \( O_2 \) delivery than between arterial saturations and \( O_2 \) delivery. However, the measurement of mixed venous saturation in clinical practice remains difficult (21).

**Limitations of the Mathematical Model**

\( \text{CVO}_2 \) was kept constant when the effect of HR was simulated. As far as the exercise physiology is concerned, the calculations of \( O_2 \) delivery and saturations were based on an \( O_2 \) consumption that was twice the baseline value. The effect of respiration on cardiopulmonary performance was not examined. However, the Frank-Starling mechanism was implemented. Other
active regulatory mechanisms were not considered in the present model.

The discrepancies between the calculated and clinical values are most likely related to the deficiencies of the latter. They result from a wide range of anatomic variations, such as anastomotic strictures, kinking, and intimal thickening, of the shunt. These will result in an overestimation of \( Q_{v}/Q_{S} \), which was our most common error. In addition, flow calculations in clinical practice are based on the measurement of mixed venous saturations (i.e., a mixture of inferior and superior vena cava blood in the right atrium). This value is not available in the Norwood patients, who have an obligatory left-to-right shunt at atrial level (all the pulmonary venous blood mixes with the systemic venous blood in the right atrium to reach the single ventricle). Minor changes in \( O_{2} \) saturations can lead to major differences in \( Q_{v}/Q_{S} \) and, thus, the deficiencies of some of these clinical data.

Finally, the mathematical model presented was not compared with specific patient cases to include a comprehensive validation of all possible clinical scenarios. In addition to the impractical aspects of manipulating physiological parameters in extremely ill children, the ethical implications of such maneuvers in the clinical setting prevented us from acquiring the necessary data. As a consequence, the model in its present form may be useful for some, but not all, patients to whom it is applied. Application of this model is further limited by the inability to predict a priori in which patients the model does not provide good correlation. However, this modeling methodology represents an important new paradigm in the analytic and numerical applications in clinical cardiopulmonary physiology. As such, it remains useful in the understanding and prediction of hemodynamic changes in these patients after their surgical reconstruction.

Conclusions

With the use of the lumped-parameter model of the Norwood circulation, the following points were demonstrated or confirmed.

With increasing shunt size a greater proportion of the CO is directed into the lungs, and this can lead to systemic hypoperfusion and poor \( O_{2} \) delivery.

Changes in SVR have a more dramatic influence on hemodynamics than changes in PVR.

Levels of oxygenation were mostly unchanged by HR. However, extremely low HRs resulted in lower \( O_{2} \) saturations.

There is a better correlation of mixed venous \( O_{2} \) saturation with systemic \( O_{2} \) delivery than of arterial saturation with \( O_{2} \) delivery.

\[ Q_{v}/Q_{S} = 1 \] results in optimal \( O_{2} \) balance and \( O_{2} \) delivery in all physiological states and shunt sizes.

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