Surgery for Congenital Heart Disease

Use of Mathematical Modeling to Compare and Predict Hemodynamic Effects Between Hybrid and Surgical Norwood Palliations for Hypoplastic Left Heart Syndrome

Tain-Yen Hsia, MD; Daria Cosentino, MS; Chiara Corsini, MS; Giancarlo Pennati, PhD; Gabriele Dubini, PhD; Francesco Migliavacca, PhD; for the Modeling of Congenital Hearts Alliance (MOCHA) Investigators

Background—Combining bilateral pulmonary artery banding with arterial duct stenting, the hybrid approach achieves stage 1 palliation for hypoplastic left heart syndrome with different flow characteristics than those after the surgical Norwood procedures. Accordingly, we used computational modeling to assess some of these differences, including influence on systemic and cerebral oxygen deliveries.

Methods and Results—A 3-dimensional computational model of hybrid palliation was developed by the finite volume method, along with models of the Norwood operation with a modified Blalock-Tausig or right ventricle–to–pulmonary artery shunt. Hybrid circulation was modeled with a 7-mm ductal stent and bilateral pulmonary artery banding to a 2-mm diameter. A 3.5-mm conduit was used in the Blalock-Tausig shunt model, whereas a 5-mm conduit was used in the right ventricle–to–pulmonary artery shunt model. Coupled to all the models was an identical hydraulic network that described the entire circulatory system based on pre–stage 2 hemodynamics. This clinically validated multiscale approach predicts flow dynamics, as well as global cardiac output, mixed venous oxygen saturation, and systemic and cerebral oxygen delivery. Compared with either of the Norwood models, the hybrid palliation had higher pulmonary-to-systemic flow ratio and lower cardiac output. Total systemic oxygen delivery was markedly reduced in the hybrid palliation (Blalock-Tausig shunt 591, right ventricle–to–pulmonary artery shunt 640, and hybrid 475 mL · min⁻¹ · m⁻²). Cerebral oxygen delivery was similarly lower in the hybrid palliation.

Conclusions—These computational results suggest that the hybrid approach may provide inferior systemic and cerebral oxygen deliveries compared with either of the 2 surgical Norwood procedures before stage 2 palliation. (Circulation. 2011;124[suppl 1]:S204–S210.)

Key Words: hypoplastic left heart syndrome ■ computer models ■ computational biology ■ palliative surgery ■ Norwood procedure

Introduced in 1993, the hybrid approach achieves stage 1 palliation for hypoplastic left heart syndrome (HLHS) by maintaining systemic perfusion through arterial ductal stenting and limiting pulmonary blood flow through bilateral surgical pulmonary artery banding. Often, an atrial septostomy or septal stenting is added to promote unobstructed pulmonary venous return. By avoiding cardiopulmonary bypass and cardiac or total circulatory arrest, the hybrid palliation procedure gained popularity initially as an option for HLHS patients for whom the surgical Norwood operation was considered high risk. However, encouraged by improved techniques and accumulated experience to overcome the early “learning curve,” some institutions have adopted the hybrid approach as the definitive strategy for stage 1 HLHS palliation. Although the procedures share common objectives, the circulatory arrangement after hybrid palliation is distinctly different from either of the 2 surgical Norwood procedures. Rather than reconstructing the right ventricular outflow with an augmented anastomosis between the pulmonary artery and aorta as in the Norwood operations, the hybrid approach achieves unobstructed systemic blood flow (Qs) by keeping the ductus arteriosus patent without aortic arch reconstruction. As a consequence, in patients with the aortic atresia variant of HLHS, as well as those with severe aortic stenosis in which antegrade flow through the aortic valve is critically limited, coronary and cerebral perfusion are dependent on retrograde filling of the aortic arch. Moreover, instead of providing pulmonary blood flow (Qp) through a shunt from either the systemic outflow or the right ventricle, the hybrid...
approach restricts pulmonary blood flow, reduces volume load, and limits diastolic runoff through banding of the branch pulmonary arteries. Therefore, the balance between Qp and Qs in the hybrid palliation is regulated in a distinctly different fashion from the surgical Norwood approaches.

Computer flow modeling has been used to examine the hemodynamic effects of a number of surgical operations, including staged reconstruction of the single ventricle. We recently applied a clinically validated multiscale computational modeling approach to highlight the hemodynamic differences between the modified Blalock-Taussig shunt (BTS) and right ventricle–to–pulmonary artery shunt (RVS) modifications of the Norwood operation. This unique investigative tool quantifies the flow dynamics in the reconstructed circulation, such as pressures and flow in the Norwood circulation, as well as global parameters such as systemic oxygen delivery. To evaluate some of the hemodynamic and physiological differences between the hybrid and the 2 surgical palliations for HLHS, multiscale models of all 3 techniques were developed.

**Methods**

The mathematical equations and computational methodologies applied in our previous multiscale modeling studies were used in the present study. Briefly, the multiscale approach couples a 3-dimensional (3D) computational fluid dynamics model of either the Norwood or the hybrid procedure to a 0-dimensional lumped parameter or hydraulic network description of the entire circulation outside the surgical domain. Figure 1 depicts the multiscale models of the hybrid, BTS, and RVS palliations. The multiscale simulation solves the flow and pressure dynamics at any part of the surgical domain of the reconstruction, such as diastolic flow reversal in the ductal stent and coronary perfusion pressure. At the same time, physiological parameters, such as systemic oxygen delivery and right ventricular stroke work, can also be calculated.

**3D Models**

Three different rigid walled 3D models of stage 1 palliation based on the finite volume method were developed. Details of the BTS and RVS models have been reported previously. For the present study, a 3.5-mm conduit was selected for the BTS model, whereas a 5-mm conduit was used in the RVS models. These models produced optimal hemodynamic and physiological results compared with the 3- and 4-mm BTS or 4- and 6-mm RVS models used in past simulations. Similarly, a hybrid model has been described recently in which the combination of a bilateral pulmonary artery banding diameter of 2 mm and a 7-mm ductal stent was shown to produce the best hemodynamic and systemic oxygen delivery performance. The ascending aorta and the transverse aortic arch were modeled to 5 mm in diameter to reflect the fact that they are not reconstructed in the hybrid approach, which also ensured that the retrograde aortic arch was not hypoplastic or restrictive. Dimensions of the pulmonary artery, coronary artery, and the 3 brachiophrenic vessels of the 3D models were the same and were obtained from angiograms of a group of patients before stage 2 palliation, as described previously. Meshes were developed with approximately 130,000 to 160,000 4-node tetrahedral volumetric elements. Blood density and viscosity were assumed equal to 1060 kg·m⁻³ and 0.005 Pa·s, respectively. The boundary conditions, segregated solvers, and implicit backward Euler method used as the time integration technique were identical for the 3 models. A minimum of 4 cardiac cycles were simulated for each computational fluid dynamics model to ensure a stable computational solution. The FLUENT general-purpose fluid dynamic code (ANYS, Inc, Canonsburg, PA) was used for the finite volume calculations.

**Lumped Parameter Network**

All lumped parameter networks coupled to the 3 models were identical and described the circulatory network of the entire body minus the 3D surgical domain. Data from 28 HLHS patients at the time of pre–stage 2 catheterization were used to construct the mathematical network. There were 5 subsystems: Heart, upper and lower systemic circulation, pulmonary circulation, and coronary circulation, similar to previously developed models. A model defined in a previous study from our laboratory was used for the heart. Time-varying elastance was used to model the right and left atria and the single right ventricle with aortic and mitral atresia.
Nonlinear resistances were adopted to describe the ventricular inflow and outflow valves, whereas a linear term models a nonrestrictive atrial septal defect. The systemic circulation is further divided into 7 arterial and venous compartments, and the pulmonary circulation into 4. Four compartments represent the coronary circulation, in which a pressure generator controlled by the right ventricular pressure produces the intramyocardial pressure. The main parameters used in all the mathematical models were as follows: Body surface area of 0.33 m$^2$, pulmonary vascular resistance of 2.3 mm Hg $\cdot$ m$^{-2} \cdot$ L$^{-1}$ $\cdot$ min$^{-1}$, heart rate of 120 bpm, hemoglobin value of 16.52 g/dL, oxygen consumption of 156.83 mL $\cdot$ min$^{-1} \cdot$ m$^{-2}$, and pulmonary venous oxygen saturation of 98%.

**Multiscale Solution**

Coupling between the 3 models described above (3D and lumped parameter), characterized by different levels of detail, was accomplished by means of interface conditions of flow rates and pressures. The infinite volume method, adopted for the multiscale models, solves the mass and momentum conservation equations for an incompressible Newtonian fluid, ie, the Navier-Stokes equations. The lumped parameter network is described by a nonlinear algebraic differential equation system that contains forcing terms derived from interface conditions with the 3D finite volume model. According to the above interface conditions, uniform time-dependent pressures were imposed at the boundaries of the 3D model, whereas the local velocity profiles were not forced but were calculated at each time instant. This allowed detection of possible reversal flows at the interfaces. Detailed sensitivity analysis to assess the validity and stability of the computational solutions and to define proper mesh and time-step conditions has been described previously in detail. All simulations were performed on an Intel Core 2 Duo 3-GHz personal computer. Time required for simulation of 1 cardiac cycle was approximately 12 hours.

On the basis of various flows obtained from the simulations, systemic and cerebral oxygen deliveries (mL of O$_2 \cdot$ min$^{-1} \cdot$ m$^{-2}$) were calculated as follows:

$$O_2^{\text{sys}}\text{delivery}=\frac{Q_S \cdot C_{aw}O_2}{\text{BSA}}$$

$$O_2^{\text{cerebral}}\text{delivery}=O_2^{\text{cerebral}}\text{delivery} \cdot \frac{Q_C}{Q_S}$$

where $Q_S$ and $Q_C$ are the systemic and cerebral volume flow rates, BSD is the body surface area, and $C_{aw}O_2$ is the oxygen arterial content. $Q_C$ was calculated as the sum of the flow rates through the left and right carotid arteries.

**Results**

For each of the 3 models, the multiscale approach provides solutions to both pressure and flow dynamics and to physiological variables, such as oxygen delivery and cardiac output. Because of the large number of potential variables that can be generated with each simulation, only those that are most clinically relevant are presented. These data are summarized in the Table. Variables derived from the 3D models include pulmonary artery pressure and flow, coronary artery flow and perfusion pressure, and Qp/Qs ratio. Cardiac output is the summation of flows between $Q_S$ and $Q_p$. Right ventricular performance can be evaluated from pressure-volume loops generated from the heart component of the lumped parameter network, including ejection fraction, stroke work, and mechanical efficiency (stroke work/total mechanical energy). Moreover, oxygen transport equations, including Equations 1 and 2 herein, can be combined with the multiscale approach, which allows for calculations of systemic and mixed venous oxygen saturations, as well as systemic and cerebral oxygen deliveries. Figures 2 and 3 graphically demonstrate differences in systemic and cerebral oxygen deliveries, as well as right ventricular pressure-volume loops, among the 3 models. Figure 4 visualizes the flow characteristics throughout a cardiac cycle in either shunt in the 2 Norwood models and in the ductal stent in the hybrid model. Comparisons between the BTS and RVS models have been described in detail previously; therefore, they will not be highlighted in the present report.

With a bilateral pulmonary artery banding diameter of 2 mm, pulmonary blood flow and pressure were accentuated in the hybrid model, which resulted in a higher Qp/Qs ratio than in either of the Norwood models; however, the cardiac output predicted in the hybrid model was lower, and coronary and cerebral perfusions through the retrograde aortic arch were substantially less than in the Norwood models. Moreover, despite a higher arterial saturation, the hybrid model showed lower mixed venous saturation. As a consequence of lower

### Table. Results of Simulations With the 3 Multiscale Models

<table>
<thead>
<tr>
<th></th>
<th>BTS Model</th>
<th>RVS Model</th>
<th>Hybrid Model</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pulmonary artery mean pressure, mm Hg</td>
<td>11.9</td>
<td>11.0</td>
<td>13.3</td>
</tr>
<tr>
<td>Pulmonary blood flow, L/min</td>
<td>1.14</td>
<td>1.05</td>
<td>1.24</td>
</tr>
<tr>
<td>Qp/Qs</td>
<td>1.0</td>
<td>0.8</td>
<td>1.4</td>
</tr>
<tr>
<td>Cardiac output, L/min</td>
<td>2.28</td>
<td>2.31</td>
<td>2.14</td>
</tr>
<tr>
<td>Coronary blood flow, L/min</td>
<td>0.076</td>
<td>0.084</td>
<td>0.064</td>
</tr>
<tr>
<td>Coronary perfusion pressure, mm Hg</td>
<td>43.3</td>
<td>64.1</td>
<td>31.4</td>
</tr>
<tr>
<td>Cerebral blood flow, L/min</td>
<td>0.26</td>
<td>0.29</td>
<td>0.19</td>
</tr>
<tr>
<td>Ejection fraction, %</td>
<td>52.5</td>
<td>61.3</td>
<td>46.1</td>
</tr>
<tr>
<td>SV mechanical efficiency</td>
<td>0.78</td>
<td>0.85</td>
<td>0.67</td>
</tr>
<tr>
<td>Stroke work, mL/mm Hg</td>
<td>2259.8</td>
<td>1967.1</td>
<td>2187.6</td>
</tr>
<tr>
<td>O$_2$ saturation, mixed venous, %</td>
<td>56.9</td>
<td>57.2</td>
<td>53.1</td>
</tr>
<tr>
<td>O$_2$ saturation, arterial, %</td>
<td>77.5</td>
<td>75.8</td>
<td>79.2</td>
</tr>
<tr>
<td>Systemic O$_2$ delivery, mL $\cdot$ min$^{-1} \cdot$ m$^{-2}$</td>
<td>590.5</td>
<td>640.0</td>
<td>475.2</td>
</tr>
<tr>
<td>Cerebral O$_2$ delivery, mL $\cdot$ min$^{-1} \cdot$ m$^{-2}$</td>
<td>133.6</td>
<td>147.7</td>
<td>100.7</td>
</tr>
</tbody>
</table>

BTS indicates modified Blalock-Taussig shunt; RVS, right ventricle-to-pulmonary artery shunt; and SV, single ventricle.
blood flow, both systemic and cerebral oxygen deliveries were considerably poorer in the hybrid model (Figure 2).

When ventricular performance was compared in terms of ejection fraction and mechanical efficiency, both Norwood models demonstrated higher values than the hybrid model. The pressure-volume loops in Figure 3 illustrate this behavior.

The presence of forward flow throughout a cardiac cycle in the BTS model has been reported previously, and backward flow in the RVS during diastole was first shown by our group and confirmed clinically. Not surprisingly, in the hybrid palliation, diastolic runoff into the branch pulmonary arteries can occur through the ductal stent, and this is predicted by the hybrid model (Figure 4). However, simulation results have also demonstrated 33% of forward flow in the brachiocephalic artery is reversed backward during diastole.

**Discussion**

Encouraged by improved collaboration between interventional cardiologists and surgeons, new technologies, and the overcoming of the learning curve that plagued earlier attempts, the hybrid stage 1 palliation is emerging as an alternative treatment strategy for patients with HLHS. Although the initial argument for the hybrid approach focused on HLHS patients who were considered high risk for conventional surgery, many groups have demonstrated increased stability in patients undergoing the hybrid procedure, including reduced ventilation time and shorter intensive care unit and hospital stays. As a consequence, there is increasing interest in adopting the hybrid approach as the primary palliation for all HLHS patients. In addition to avoiding the myocardial dysfunction and instability of systemic and pulmonary vascular resistance associated with surgical Norwood operations, the hybrid palliation has other advantages, including provision of a pulmonary blood flow that is not dependent on a shunt from the systemic circulation or a right ventricular incision. However, pulmonary artery banding can accentuate right ventricular afterload and lead to significant myocardial injury, and reproducible optimal regulation of pulmonary blood flow through bilateral branch banding remains difficult to achieve. Notwithstanding these differences, the goal of the hybrid management is not unlike that of the surgical strategies: To effectively palliate HLHS patients through the neonatal period with minimal morbidity and mortality, preserving ventricular function while allowing normal growth and development, especially in the pulmonary vascular bed. However, questions remain as to whether the hybrid approach leads to equivalent palliation as the conventional Norwood operations. Although an ongoing randomized controlled trial aims to answer this question, the present study, adopting the recently introduced and validated multiscale modeling approach, aimed to mathematically examine some of the hemodynamic and physiological differences between the hybrid approach and Norwood operations.

The present mathematical modeling investigation demonstrates that the hybrid palliation of HLHS results in a distinct hemodynamic characteristic that is different from either of the 2 surgical Norwood procedures. Despite banding of the branch pulmonary arteries to 2 mm, simulation results predicted higher pulmonary blood flow and lower cardiac output after hybrid palliation. As a consequence of lower systemic blood flow and the obligatory retrograde perfusion through an unreconstructed aortic arch, coronary and cerebral blood flows were substantially less than those achieved in the Norwood circulations. Most importantly, both systemic and cerebral oxygen deliveries were reduced in the hybrid model; therefore, despite higher arterial oxygen saturations, mixed venous saturation was lower. Moreover, the hybrid model exhibited diastolic runoff through the ductal stent, which resulted in flow reversal in the brachiocephalic artery, which exacerbated the reduction in cerebral perfusion. Taken together, the multiscale simulation results suggest that compared with the 2 surgical Norwood operations, the hybrid approach would produce a hemodynamically poorer stage 1 palliation.

Although ductal patency can be fairly reliably maintained with modern stent technology, it was recognized early that the restriction of pulmonary blood flow through bilateral branch pulmonary artery banding could be particularly challenging in HLHS patients. Bands that were too loose could lead to pulmonary overcirculation, whereas those that were too tight would produce unacceptable cyanosis. Either would result in suboptimal systemic oxygen delivery. Therefore, in our first investigation into the hemodynamics of the hybrid procedure, the effect of banding size was assessed. Even with bilateral pulmonary artery bands of 2-mm diameter, which resulted in the highest oxygen delivery and optimal hemodynamics in our simulations, the Qp/Qs ratio remained higher than that achieved in the 2 Norwood models. This finding is in agreement with a recent study of postoperative stage 1 hemodynamics in which the mean Qp/Qs ratio was 1.8 in patients who underwent the hybrid procedure, whereas 28% of the patients had a Qp/Qs ratio of >2:1 and 11% had a ratio of >3:1. The difficulty in reproducibly restricting pulmonary blood flow through bilateral banding would likely accentuate the suboptimal systemic and cerebral oxygen deliveries in patients undergoing the hybrid procedure.

The combination of the obligatory volume load on the single ventricle and the additional afterload brought on by bilateral pulmonary artery banding would explain the poorer ventricular performance in the hybrid model. In addition to lower ejection fraction and right ventricular mechanical
Figure 4. Velocity profiles on various cross sections of the shunts and the ductus arteriosus in the modified Blalock-Taussig shunt (BTS; top), right ventricle-to-pulmonary artery shunt (RVS; middle), and hybrid (HYB; bottom) models at 4 time points in the cardiac cycle.
efficiency in the hybrid model, the pressure-volume loops generated from the heart component of the multiscale model also predicted a high stroke work, which suggests high ventricular wall stress. Moreover, compared with the hybrid model, the right ventricles in both Norwood models had reduced afterload. This feature of the Norwood models permits larger right ventricular output, which provides higher oxygen delivery despite lower pulmonary blood flow and arterial saturation than in the hybrid model. Also, the reduced end-diastolic volume of the right ventricle would produce a slight reduction in atrial pressure, which combined with lower pulmonary blood flow would result in lower mean pulmonary artery pressure in the Norwood models.

Retrograde aortic arch obstruction has been realized as an important complication of hybrid palliation, with an incidence of 10% to 24%, and in some centers, preintervention recognition of a substrate for obstruction is a contraindication to the hybrid approach.\(^\text{22}\) In the present study, the retrograde aortic arch was modeled to 5 mm in diameter to eliminate the influence of hypoplasia or isthmus obstruction. Despite this, cerebral and coronary flows were lower than in the surgical Norwood models, in which antegrade flow is promoted through the augmented aortic reconstruction. Whether the retrograde aortic arch, even without obstruction, contributes to reduced coronary and cerebral perfusion is a question that can have important outcome implications and will require further clinical investigation. Lastly, we did not model a recent modification to the hybrid palliation proposed by a group from The Hospital for Sick Children in Toronto, Canada, in which a shunt between the main pulmonary artery and the brachiocephalic artery was added to provide additional blood flow into the retrograde aortic arch.\(^\text{24}\) Whether this “reverse” modified BTS would ameliorate the reduced cerebral and coronary perfusion in the hybrid model is under investigation.

Despite the advantages of being able to correlate local pressure and the flow effects of stage 1 palliation strategies with systemic physiological parameters, the multiscale modeling approach used in the present report has several limitations. Present mathematical modeling studies, including ours, remain unable to completely account for biological adaptation and cardiovascular autoregulation, including the coronary circulation. For example, the effect of cyanosis on myocardial function and vascular tone cannot be simulated. Ventricular adaptation to different volume loading conditions is not well understood and may variably affect the resulting right ventricular performance both acutely and chronically. The hemodynamic variables used to construct the multiscale models were obtained from clinical investigations of patients before superior cavopulmonary connections were established and therefore are not reflective of intraoperative or early postoperative conditions. However, by simulating late interstage conditions, the modeling examines the effects of the 3 stage 1 palliations on pre–stage 2 hemodynamics and physiology. As mentioned previously, the immediate goal of either the hybrid or surgical palliation approach is to optimize interstage physiology and limit morbidity and mortality before second-stage conversion. Finally, multiscale simulations are computationally demanding and do not allow for extensive use in clinical care. Therefore, we are developing a simplified lumped parameter description that can provide fast and reliable solutions for single-ventricle palliations.

**Conclusions**

The multiscale modeling approach indicates that with optimal bilateral pulmonary artery banding and a good-sized retrograde aortic arch, hybrid palliation can lead to higher pulmonary blood flow and lower cardiac output than either the BTS or RVS modifications of the Norwood operation. Moreover, both systemic and cerebral oxygen deliveries are lower in the hybrid palliation, with poorer ventricular performance. Diastolic runoff through the ductal stent can occur and can cause flow reversal in the brachiocephalic circulation. Although these results do not predict inferior clinical outcomes with hybrid palliation, they can be a useful addendum to shed mechanistic insights into observations derived from randomized trials.

**Appendix**

**MOCHA Investigators**

Andrew Taylor, MD, Alessandro Giardini, MD, Sachin Khambadkone, MD, Silvia Schievano, PhD, Marc de Leval, MD, and T-Y. Hsia, MD (Institute of Child Health, London, United Kingdom); Edward Bove, MD, and Adam Dorfman, MD (University of Michigan, Ann Arbor, MI); G. Hamilton Baker, MD, and Anthony Hlavacek (Medical University of South Carolina, Charleston, SC); Francesco Migliavacca, PhD, Giancarlo Pennati, PhD, and Gabriele Dubini, PhD (Politecnico di Milano, Milan, Italy); Alison Marsden, PhD (University of California, San Diego, CA); Irene Vignon-Clementel (National Institute of Research in Informatics and Automation, Paris, France); and Richard Figliola, PhD, and John McGregor, PhD (Clemson University, Clemson, SC).

**Sources of Funding**

The present study was supported by a grant from the Fondation Leducq, Paris, France.

**Disclosures**

None.

**References**


6. Bove EL, de Leval MR, Migliavacca F, Guadagni G, Dubini G. Computational fluid dynamics in the evaluation of hemodynamic performance of


Use of Mathematical Modeling to Compare and Predict Hemodynamic Effects Between Hybrid and Surgical Norwood Palliations for Hypoplastic Left Heart Syndrome

Tain-Yen Hsia, Daria Cosentino, Chiara Corsini, Giancarlo Pennati, Gabriele Dubini, Francesco Migliavacca and for the Modeling of Congenital Hearts Alliance (MOCHA) Investigators

_Circulation_. 2011;124:S204-S210
doi: 10.1161/CIRCULATIONAHA.110.010769

_Circulation_ is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 2011 American Heart Association, Inc. All rights reserved.
Print ISSN: 0009-7322. Online ISSN: 1524-4539

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://circ.ahajournals.org/content/124/11_suppl_1/S204