The total cavopulmonary connection resistance: a significant impact on single ventricle hemodynamics at rest and exercise

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Sundareswaran KS, Pekkan K, Dasi LP, Whitehead K, Sharma S, Kanter KR, Fogel MA, Yoganathan AP. The total cavopulmonary connection resistance: a significant impact on single ventricle hemodynamics at rest and exercise. Am J Physiol Heart Circ Physiol 295: H2427–H2435, 2008. First published October 17, 2008; doi:10.1152/ajpheart.00628.2008.—Little is known about the impact of the total cavopulmonary connection (TCPC) on resting and exercise hemodynamics in a single ventricle (SV) circulation. The aim of this study was to elucidate this mechanism using a lumped parameter model of the SV circulation. Pulmonary vascular resistance (1.96 ± 0.80 WU) and systemic vascular resistances (18.4 ± 7.2 WU) were obtained from catheterization data on 40 patients with a TCPC. TCPC resistances (0.39 ± 0.26 WU) were established using computational fluid dynamic simulations conducted on anatomically accurate three-dimensional models reconstructed from MRI (n = 16). These parameters were used in a lumped parameter model of the SV circulation to investigate the impact of TCPC resistance on SV hemodynamics under resting and exercise conditions. A biventricular model was used for comparison. For a biventricular circulation, the cardiac output (CO) dependence on TCPC resistance was negligible (sensitivity = −0.064 1·min⁻¹·WU⁻¹) but not for the SV circulation (sensitivity = −0.88 1·min⁻¹·WU⁻¹). The capacity to increase CO with heart rate was also severely reduced for the SV. At a simulated heart rate of 150 beats/min, the SV patient with the highest resistance (1.08 WU) had a significantly lower increase in CO (20.5%) compared with the SV circulation as a whole using computational fluid dynamic simulations conducted on anatomically accurate three-dimensional models reconstructed from MRI (119%). This was due to the increased afterload (Ea) and decreased cardiac function. Senzaki and colleagues (35) argued that increased Ea decreased preload (Ees: ventricular filling), and abnormal ventricular-vascular-coupling are contributing factors for the decreased cardiac reserve and function in patients with a Fontan circulation. A study by Szabo et al. (40) reported increased Ea and decreased Ees as well using pressure-volume analysis conducted on measurements made in a dog SV model. In addition to experimental studies, theoretical models have also predicted similar changes in Ees, Ees, and cardiac reserve in a Fontan circulation (14, 22, 28).

Most of the studies thus far on the Fontan circulation can be broadly categorized into two types: 1) those that study the Fontan circulation as a whole using in vivo animal and human studies (35, 36, 40); and 2) those that study the fluid mechanics of the surgically created TCPC in isolation from the SV circulation (27, 41, 42). There have not been many studies that have connected the two, i.e., those that relate the hemodynamics of the TCPC to upstream hemodynamics and cardiac function. Furthermore, no study to date has quantified TCPC resistances in actual patient TCPCs, which has proved to be a caveat for understanding the true magnitude of TCPC in the context of pulmonary vascular resistance (PVR) and systemic vascular resistance (SVR).

Therefore, the primary objective of this study was to quantify the impact of the hemodynamic resistance induced by the geometry of the TCPC on two critical aspects of the Fontan circulation: 1) exercise performance and 2) cardiac function. For the first time, TCPC hemodynamics were studied in context of the entire SV circulation using clinically acquired magnetic resonance images and cardiac catheterization data on Fontan patients.

METHODS

Patient Data

A multicenter Fontan patient cardiac MRI database of over 200 patients was established to study anatomic elements of the TCPC.

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Acquisitions consisted of a stack of axial anatomic images for the reconstruction of geometry, and cine phase contrast (PC) MRI acquisitions for flow quantification at the superior vena cava (SVC), inferior vena cava (IVC), left pulmonary artery (LPA), and right pulmonary artery (RPA). Informed consent was obtained, and all associated experiments were approved by the Internal Review Boards of the Children’s Hospital of Philadelphia, the Children’s Healthcare of Atlanta, and Georgia Institute of Technology.

Three-dimensional anatomic and flow reconstructions of the TCPC were generated using techniques previously developed and validated (9). From this database, 16 patient-specific geometries (6 intra-atrial, 9 extra-cardiac, and 1 IVC-main pulmonary artery) were selected for computational fluid dynamic (CFD) simulations. The selected geometries are shown in Fig. 1. Table 1 shows the clinical data associated with each model selected in the study as well as the resting COs obtained from PC MRI. In addition, cardiac catheterization data were also available on 40 patients with a SV physiology, which were used for estimating the vascular parameters for the systemic and pulmonary circulations. Specifically, SVR and PVR measurements were used in the mathematical model, whereas pressure and flow measurements were used for validating the model.

**CFD Simulations**

Three-dimensional anatomic reconstructions were used for grid generation in which vessel volumes were divided into computational elements (meshes). The number of elements varied depending on geometry size and complexity and ranged from 548,842 to 1,674,440 for the models studied. At each element, the governing Navier-Stokes conservation equations of mass and momentum for laminar fluid flow were solved using FLUENT (Fluent, Lebanon, OH). All solutions were obtained using second-order solvers assuming a Newtonian fluid with a density of 1.060 kg/m³ and viscosity of 3.71 \( \text{e}^{-3} \text{N}\cdot\text{s}\cdot\text{m}^{-2} \). The patient-specific TCPC CFD analysis methodology and in vitro validations of these techniques have been described in previous studies (27, 29, 42). For each patient geometry, blood flow was modeled at baseline steady-state flow conditions by setting SVC and IVC flows to values derived from PC MRI averaged over the cardiac cycle. Outflows were defined by pressure boundary conditions, with values tuned to obtain the desired pulmonary flow splits at the equal vascular lung resistance condition, as previously described (27). To determine the resistance of the TCPC under exercise conditions, simulations were also conducted as 1 l/min increases for younger patients (3–7 yr) and two times and three times the resting flow rates for older patients (>7 yr), with the only exception being model M15.

**TCPC Resistance Evaluation**

CFD simulations were used to provide pressure and flow measurements throughout the TCPC pathway. Using the measurements at the inlets (SVC and IVC) and outlets (LPA and RPA), the control volume energy loss \( (E_{\text{Loss}}) \) was computed according to the following equation:

\[
E_{\text{Loss}} = P_{\text{SVC}} \times Q_{\text{SVC}} + P_{\text{IVC}} \times Q_{\text{IVC}} - P_{\text{LPA}} \times Q_{\text{LPA}} - P_{\text{RPA}} \times Q_{\text{RPA}}
\]

where \( P \) is pressure and \( Q \) is flow. An energy loss-based pressure drop

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Fig. 1. Three-dimensional anatomic reconstructions of the total cavopulmonary connection (TCPC) models used in this study. In total, there were six intra-atrial models (models M01, M03, M04, M05, M14, and M15), nine extracardiac models (models M02, M06, M07, M08, M09, M10, M12, M13, M16), and one inferior vena cava-main pulmonary artery TCPC model (model M11).
Table 1. Clinical data of patients used in the study

<table>
<thead>
<tr>
<th>Model</th>
<th>Type of Congenital Heart Disease</th>
<th>Fontan Type</th>
<th>Age, yr</th>
<th>Simulation Conditions, l/min</th>
</tr>
</thead>
<tbody>
<tr>
<td>M01</td>
<td>HLHS</td>
<td>IA</td>
<td>12</td>
<td>2, 4, and 6</td>
</tr>
<tr>
<td>M02</td>
<td>DORV, PA</td>
<td>EC (BL)</td>
<td>9</td>
<td>2.5, 7.5, and 7.5</td>
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<tr>
<td>M03</td>
<td>HLHS</td>
<td>IA</td>
<td>18</td>
<td>2.4, 4.8, and 7.2</td>
</tr>
<tr>
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<td>TA</td>
<td>IA</td>
<td>10</td>
<td>2.9, 5.8, and 8.7</td>
</tr>
<tr>
<td>M05</td>
<td>PA, HRHS</td>
<td>IA</td>
<td>15</td>
<td>2.75, 5.5, and 8.25</td>
</tr>
<tr>
<td>M06</td>
<td>Heterotaxy, DC</td>
<td>EC (BL)</td>
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<td>2.37, 4.72, and 4.37</td>
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<tr>
<td>M07</td>
<td>DILV, TGA</td>
<td>EC</td>
<td>9</td>
<td>3.5, 7, and 10.5</td>
</tr>
<tr>
<td>M08</td>
<td>DC, TA</td>
<td>EC</td>
<td>3</td>
<td>2.7, 3.7, and 4.7</td>
</tr>
<tr>
<td>M09</td>
<td>TA</td>
<td>EC</td>
<td>7</td>
<td>3.03, 6.06, and 9.09</td>
</tr>
<tr>
<td>M10</td>
<td>PA, HRHS</td>
<td>EC</td>
<td>8</td>
<td>3, 6, and 9</td>
</tr>
<tr>
<td>M11</td>
<td>DORV, EC</td>
<td>IVC – MPA</td>
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<td>3, 4, and 5</td>
</tr>
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<td>HLHS</td>
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<td>EC</td>
<td>5</td>
<td>3, 4, and 5</td>
</tr>
<tr>
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<td>SV, DIAV</td>
<td>IA</td>
<td>3</td>
<td>2, 3, and 4</td>
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<td>HLHS</td>
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<td>11</td>
<td>4, 6, and 7</td>
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<tr>
<td>M16</td>
<td>HLHS</td>
<td>EC</td>
<td>6</td>
<td>2, 3, and 4</td>
</tr>
</tbody>
</table>

Shown are the diagnosis and simulation conditions of the models used in this study. HLHS, hypoplastic left heart syndrome; DORV, double outlet left ventricle; PA, pulmonary atresia; TA, tricuspid atresia; HRHS, hypoplastic right heart syndrome; DC, dextrocardia; DILV, double inlet atrioventricular connection; TGA, transposition of the great arteries; IA, intra-atrial; EC, extracardiac; BL, bilateral; IVC, inferior vena cava; MPA, main pulmonary artery.

The advantage of such a mathematical model is that additional chambers or shunts can be introduced into the system, which is an option particularly valuable in congenital heart defect research. The instantaneous flow and pressure from compartment i to compartment j were then evaluated by solving the following set of differential equations:

\[
\frac{d(CP_i)}{dr} = \sum_{j=1}^{N} j(Q_{ij} - Q_{ji})
\]

Here, the subscript \(ij\) depicts the flow from compartment i to compartment j, where compartment j is a compartment after compartment i. \(P_i, Q_i, \) and \(C_i\) are the pressures, flows, and compliances in compartment i; \(R_{ij}, L_{ij},\) and \(S_{ij}\) are the resistances, lumped impedances, and switches enforcing the directionality of flows, respectively. \(N\) is the number of chambers in the model. Vascular resistance values were obtained from cardiac catheterization data; impedance and compli-
ance values were obtained from the literature. The differential equation was solved iteratively for each chamber until the results converged.

The atria and ventricles themselves were modeled as time-varying compliance chambers generating activation energies similar to those described by Sun et al. (39). Pulsatile pressure was generated in these models via functions that alternate between systolic (stiff) and diastolic (relaxed) ventricular activation functions. These activation functions govern the systolic and diastolic contraction properties of the myocardial muscle. Compliances were then used along with Eq. 4 for generating the pressure waveforms within the four chambers of the heart, respectively. The following equations were used for generating the compliances:

\[
E(t) = \frac{1 - e^{-t/T_s}}{1 - e^{-t/T_r}}, \quad 0 \leq t \leq T_s \\
CV(t) = CVD \times (CVS/CVD)^{E(t)} \\
E(t) = \frac{1 - e^{-(t-T_s)}}{1 - e^{-(t-T_r)}}, \quad T_s \leq t \leq T \\
CV(t) = CVS \times (CVS/CVS)^{E(t)}
\]

\(E\) is the load of each chamber, \(T_s\) (0.0025 min) and \(T_r\) (0.0075 min) are the time constants governing the contraction and relaxation of the myocardial muscle during systole and diastole. \(T\) is the duration of one cardiac cycle (1/heart rate), \(T_s\) is the length of systole (T73 at rest and T72 at exercise), and \(t\) is the current point in the cardiac cycle. Systole and diastole were switched for modeling atrial contraction. CVD and CVS were the minimum and maximum compliance values (CVs) of the chamber. The valves were modeled as linear unidirectional resistors with a resistance of 0.01 WU. Please note that 1 WU is equivalent to 1 mmHg·1·min⁻¹ and is a commonly used clinical parameter to describe resistance to blood flow. The parameter values used in Eq. 5 for each heart chamber are shown in Table 3.

### Modeling Rest/Exercise Conditions and Data Analysis

**Rest.** To simulate the impact of TCPC resistance on CO, \(R_{TCPC}\) in the model was uniformly varied from 0 to 1.8 WU (from 0 to 90% PVR), and its corresponding effect on CO for the biventricular and univentricular circulations was evaluated. The range of \(R_{TCPC}\) was selected based on the computational models described above and used to evaluate the sensitivity of the model to \(R_{TCPC}\). For the biventricular circulation, since there is no TCPC, the PVR was increased by an equivalent amount. In addition, pressure-volume analysis was conducted for a normal subject and TCPC cases with the highest, mean, and lowest resistances to demonstrate how the operating point of the univentricular circulation changes with resistance.
EXERCISE CONDITION 3. There is also a significant impact of the pulmonary system and lungs during exercise, especially in Fontan patients, where the negative intrathoracic pressure greatly augments flow. Studies have reported a 40% drop in the PVR as a result of this phenomenon in addition to the local vasodilation that occurs to improve exercise tolerance (1). Therefore, the PVR in our model was gradually dropped from 1.96 WU, as measured from the catheterization data, to 1.1 WU, based on the severity of exercise.

EXERCISE CONDITION 4. As the CO increases with increasing heart rate, so does $R_{TCPC}$. Figure 3 shows the dynamic range of $R_{TCPC}$ values and how they change between the different geometries. As can be observed, there is a nonlinear increase in resistance with CO. This phenomenon becomes important during elevated CO conditions. To take this characteristic into account, $R_{TCPC}$ was treated as a dynamic element that increased with an increase in CO. The $R_{TCPC}$ curves shown in Fig. 3 were used to evaluate the correct resistance for each exercise condition.

Based on these exercise conditions, the following parameters were evaluated as a function of heart rate for the normal and SV circulations, respectively: CO, end-systolic pressure, central venous pressure (CVP), $E_a$, $E_{es}$, the ventricular-vascular coupling ratio ($E_a/E_{es}$), $R_{TCPC}$, and the ratio of $R_{TCPC}$ to PVR ($R_{TCPC}/PVR$). Pressure-volume loops were used to evaluate the slope of the end-systolic volume elastance, or $E_a$, and the vascular $E_{es}$ property. These parameters were evaluated based on the methodology outlined by Nogaki et al. (22). All authors had full access to the data and take responsibility for its integrity. All authors read and agreed to the manuscript as written.

RESULTS

SV Resistance

The average age and body surface area of the patients used in this study were $8.25 \pm 4.28$ yr (minimum: 2 yr and maximum: 18 yr) and $0.97 \pm 0.28$ m² (minimum: 0.54 m² and maximum: 1.49 m²), respectively. Measured PVR was $1.96 \pm 0.80$ WU (minimum: 1 WU
Fig. 5. Impact of increasing heart rate on cardiac output (A), end-systolic pressure (B), central venous pressure (C), ventricular $E_a$ (D), ventricular $E_{es}$ (E), vascular-ventricular coupling (F), $R_{TCPC}$ (G), and $R_{TCPC}$/pulmonary vascular resistance (PVR) (H) for the case of a normal biventricular circulation (●) and single ventricle scenarios with a low-resistance TCPC (■), mean-resistance TCPC (○), or high-resistance TCPC (▲).
The changes in $R_{TCPC}$ during exercise for the models used in the study. $R_{TCPC}$ values were $0.39 \pm 0.26$ WU (minimum: 0.1 WU and maximum: 1.08 WU) during rest, $0.70 \pm 0.45$ WU (minimum: 0.13 WU and maximum: 1.72 WU) during moderate exercise, and $1.06 \pm 0.73$ WU (minimum: 0.18 WU and maximum: 2.65 WU) during severe exercise. The most efficient TCPCs at rest and exercise were models M7 and M9, respectively. The least efficient TCPCs at rest and exercise were models M13 and M17. $R_{TCPC}$ values were evaluated to be significant percentages of the measured PVR (22% at rest).

Intra-atrial TCPCs had higher resistances ($0.43 \pm 0.12$ WU; minimum: 0.24 WU and maximum: 0.59 WU) compared with extra-cardiac TCPCs ($0.35 \pm 0.35$ WU; minimum: 0.1 WU and maximum: 1.08 WU), although this was not statistically significant. The results were skewed due to the presence of an outlier in model M12 for the extra-cardiac case. If this outlier is removed from the analysis, then the results do become statistically significant at $P < 0.05$.

**Lumped Parameter Model Validation**

For a simulated resting heart rate of 70 beats/min and an average $R_{TCPC}$ of 0.39 WU, systolic/diastolic aortic pressures were 117/85 mmHg and 115/73 mmHg for the normal and SV cases, respectively. The lower diastolic pressures resulted in a lower mean aortic pressure of 95 mmHg (compared with 103 mmHg) for the SV circulation. CO was significantly lower for the SV circulation at 3.8 compared with 5.1 l/min for the normal circulation. This can be attributed to the increased $E_s$ experienced by the SV due to the lack of a pumping chamber on the right side. Pulmonary artery pressures were nonpulsatile in the SV circulation, which resulted in nonpulsatile flow in the pulmonary arteries, which was in correlation with previous clinical studies. Table 4 shows a comparison of the modeled hemodynamic data versus observed data from cardiac catheterization performed on 40 patients with a SV physiology. There was a good match between what was predicted by the model and what was observed clinically, demonstrating the validity of the model used for this study.

**Effect of $R_{TCPC}$ at Rest**

Figure 4 shows the impact of $R_{TCPC}$ on hemodynamics in a SV and normal circulation at a resting heart rate of 70 beats/min. There was a drop in CO going from a biventricular to univentricular circulation at zero resistance, which was due to the lack of a systemic ventricle and the serial configuration of the two circulations. The sensitivity of CO to $R_{TCPC}$ in the SV was $-0.88$, which was significantly higher compared with $-0.064$ for the normal biventricular circulation. This implies that for every 10% increase in resistance, there is an 8.8% drop in CO. Figure 4C shows the impact of $R_{TCPC}$ on CVP. The sensitivity of CVP to increase in $R_{TCPC}$ was 0.64, implying that a 10% increase in resistance results in a 6.4% increase in CVP. The increase in CVP in the SV has been previously shown using acute in vivo animal experiments (40), human experiments (35), and theoretical experiments (14, 22). However, the impact of the TCPC procedure on CVP was shown for the first time in this study.

**Effect of $R_{TCPC}$ During Exercise**

Figure 5 shows hemodynamic responses to exercise as predicted by the model. The biventricular circulation was able to increase the CO of 5.1 l/min at a heart rate of 70 beats/min to 11.4 l/min at an exercise heart rate of 150 beats/min (Fig. 5A). This ability to increase CO was blunt in the SV circulation. In the SV, the increase in CO was only from 3.8 to 5.4 l/min for a mean $R_{TCPC}$ of 0.39 WU, from 4.4 to 6.8 l/min for the TCPC with a minimum resistance of 0.1 WU, and from 3.3 to 4.1 l/min for a highly dissipative TCPC with a resistance of 1.08 WU. There was an increase in end-systolic pressure with exercise for the biventricular circulation but not for the SV circulation (Fig. 5B). The CVP was consistently higher for the TCPC with high resistance (Fig. 5C).

The $E_s$ experienced by the SV significantly increased with exercise compared with the biventricular circulation (Fig. 5D). The presence of a highly dissipative TCPC further increased $E_s$. The increases were from 1.65, 1.62, and 1.7 mmHg/ml to 2.23, 2.14, and 2.54 mmHg/ml for mean, minimum, and maximum $R_{TCPC}$ values, respectively. Although similar at rest, the differences increased with exercise. In comparison, $E_s$ only increased from 1.46 to 1.87 mmHg/ml for the biventricular circulation. Ventricular $E_s$ increased (3.63 to 4.39 mmHg/ml) in the normal circulation, whereas it decreased in the case of the SV circulation (Fig. 5E). For the three SV scenarios, $E_s$ dropped from 3.12, 3.40, and 2.79 mmHg/ml to 2.73, 3.24, and 2.26 mmHg/ml for mean, minimum, and maximum $R_{TCPC}$ values, respectively. This resulted in a mismatch in the $E_s$ and $E_s$ by the ventricle, resulting in an abnormal increase in the ventricular vascular coupling ratio ($E/E_{int}$) for the univentricular circulation, which was further worsened by the presence of a TCPC with high resistance. While the $E/E_{int}$ almost remained flat for the biventricular circulation, it increased for the univentricular circulation (Fig. 5F). The increases were from 0.53, 0.48, and 0.61 mmHg/ml to 0.82, 0.66, and 1.05 mmHg/ml for mean, minimum, and maximum $R_{TCPC}$ values, respectively.

Finally, a human study (1) established that PVR and SVR go down with exercise. However, $R_{TCPC}$ increases with exercise, as shown in Fig. 3, implying that the TCPC bottleneck becomes more significant during exercise. Figure 5, G and H, demonstrate that, although at rest $R_{TCPC}$ is a fraction of PVR (22%), this fraction significantly increases with exercise (50%). In fact, for the TCPC with a high resistance, this fraction increased from 55% at rest to 155% during exercise, whereas for the TCPC with a low resistance, this change was minimal, going from 7% to 16%. This demonstrates the significant improvement that can be accomplished by optimizing TCPC geometry.

**DISCUSSION**

This study demonstrated that the TCPC, which is in series with PVR and SVR, plays a significant role in regulating CO and exercise performance in the SV. It brings to forefront that $R_{TCPC}$ is not trivial compared with downstream PVR and that any obstruction in TCPC pathway can have a more significant impact on cardiac function of a SV circulation than a biventricular circulation. Most studies until now have only demonstrated this phenomenon in a global sense by looking at the SV circulation as a whole (22–24, 35, 36, 40), and the hydrodynamic role of the TCPC was not investigated in these studies. This study shows, for the first time, using mathematical modeling with patient-specific imaging, flow simulations, and cardiac catheterization measurements, the important role played by the surgically altered TCPC geometry and the mechanism
by which it impacts the resting and exercise hemodynamic capacity of patients with a Fontan physiology.

The reduced capacity to increase CO with exercise in SV circulations has been well documented in the literature (5, 15, 17, 23). However, the exact quantitative relationship between $R_{\text{TCPC}}$ and this phenomenon has been unclear, primarily because of two reasons: 1) lack of appropriate methods for quantifying TCPC efficiency and 2) the complex interrelationships that exist between the respiratory, skeletal, and cardiovascular system that make it difficult to establish correlations between the TCPC and exercise capacity. Therefore, there is a tendency to discount the impact of the TCPC on exercise as negligible. Although PVR drops as a result of exercise, the increased $R_{\text{TCPC}}$ with increasing CO makes it the primary bottleneck during increased cardiovascular demand.

The significant variability of Fontan geometries translates to significant variability in resistances. The resistance of the “worst” TCPC was 10 times higher than the resistance of the “best” TCPC. This suggests that the TCPC procedures performed today are far from optimal, and more emphasis needs to be given for optimizing the geometries preoperatively, especially, since the sensitivity of the univentricular circulation to changes in resistance is quite significant, with a 10% increase in resistance resulting in an 8.8% decrease in CO. To verify if this phenomenon is observed in vivo, the cardiac index measured using PC MRI was plotted against the resistance evaluated using CFD for all the patients in this study (Fig. 6). Clearly, a weak but significant ($P < 0.05$) negative correlation can be observed between $R_{\text{TCPC}}$ and the resting cardiac index measured in these patients. It should be noted that $R_{\text{TCPC}}$ (as defined in the present study) is independent of downstream PVR. The only dependence is indirect, as PVR can regulate CO and $R_{\text{TCPC}}$ changes with CO (Fig. 4). Outside of this phenomenon, $R_{\text{TCPC}}$ is largely governed by geometry and the surgeon’s decision at the time of the surgery.

This study sought to bring to the clinician’s attention the following messages: 1) final-stage TCPC surgery has not yet been optimized, which is evident from the significant variability in the observed resistances; and 2) the resistance of the TCPC itself is not secondary to PVR, as commonly believed, and physiologically it plays a greater role when going from rest to exercise. Herein lies the clinical significance of the study. $R_{\text{TCPC}}$ is directly proportional to $E_s$ (as higher systolic pressures are needed to maintain CO for TCPCs with higher resistance) and inversely proportional to $E_{es}$ (as higher pressure drops across the TCPC result in lower filling pressures). This observation points toward a unique property of the SV circulation: both $E_{es}$ and $E_s$ are impacted in identical manner by the TCPC as the pulmonary ventricle is replaced by a dynamic resistance in the form of the TCPC.

Not only does optimizing $R_{\text{TCPC}}$ improve cardiac function, but it drops CVP, which is critical to maintaining normal gastrointestinal function. In addition, optimal TCPC geometries have improved flow dynamics in the baffle that may reduce the risk of thromboembolic complications. Hence, new TCPC designs that reduce energy losses need to be investigated in more detail, and more emphasis needs to be given for improving the hemodynamic efficiency within the TCPC. Surgical planning approaches combining preoperative MRI, CFD, and the presented lumped parameter model can prove to be beneficial in determining the optimum TCPC geometries. Previous studies on surgical planning and TCPC geometric optimization studies have shown that significant improvements with reductions of >50% in energy losses can be accomplished (4, 6, 7, 33, 37, 38). If appropriate surgical planning strategies are used, then it is possible to accomplish similar improvements in energy losses in vivo as well.

**Limitations**

Although our model has a sound basis in clinically measured data and compares well with other clinical studies, the inherent limitations of this work are well acknowledged. Primarily, the resting and exercise hemodynamic conditions are modeled and are not empirically observed data. Specifically, the biochemical response to exercise, cardiopulmonary interactions, and baroreflex response have not been modeled in order to achieve a simpler model with less variables. Since this is more of a comparative study between different SV circulations and the biventricular circulation, the only parameter that was changed between different cases was $R_{\text{TCPC}}$. Incorporating a more complex model will no doubt improve the accuracy of the model’s predictions, but the relative impact of $R_{\text{TCPC}}$ as illustrated here, is not expected to change.

**Conclusions**

This is the first time the impact of TCPC surgical resistance on overall hemodynamics of the univentricular circulation has been demonstrated. $R_{\text{TCPC}}$ has a direct impact on $E_s$ and $E_{es}$ of the univentricular circulation and significantly impacts resting and exercise hemodynamics. The inability to increase CO with exercise limits patients’ ability to exercise and hence worsens their overall functional outcome. This can be countered by optimizing the geometry of the TCPC before the Fontan surgery, which may result in decreased $E_s$ and, consequently, an improvement in cardiac function.

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