Pulmonary hepatic flow distribution in total cavopulmonary connections: extracardiac versus intracardiac.

Lakshmi P. Dasi  
*Colorado State University - Fort Collins*

Kevin Whitehead  
*Children's Hospital of Philadelphia*

Kerem Pekkan  
*Carnegie Mellon University, kpekkan@andrew.cmu.edu*

Diane de Zélicourt  
*Georgia Institute of Technology*

Kartik S. Sundareswaran  
*Georgia Institute of Technology*

*See next page for additional authors*

Follow this and additional works at: [http://repository.cmu.edu/bme](http://repository.cmu.edu/bme)

Part of the [Biomedical Engineering and Bioengineering Commons](https://repository.cmu.edu/bme)

Published In  
PULMONARY HEPATIC FLOW DISTRIBUTION IN TOTAL CAVOPULMONARY CONNECTIONS: EXTRA CARDIAC VS INTRA CARDIAC

Lakshmi P. Dasi, Kevin Whitehead, Kerem Pekkan, Diane de Zellicourt, Kartik Sundareswaran, Kirk Kanter, Mark A. Fogel, and Ajit P. Yoganathan

1. Department of Mechanical Engineering & School of Biomedical Engineering, Colorado State University, Fort Collins, CO
2. Division of Cardiology, Children’s Hospital of Philadelphia, Philadelphia, PA
3. Carnegie Mellon University, Pittsburg, PA
4. Wallace H. Coulter School of Biomedical Engineering, Georgia Institute of Technology, Atlanta, Georgia
5. Emory University, Atlanta, GA

Abstract

Background—Pulmonary arteriovenous malformations (PAVMs) can occur after the Fontan and are believed to be associated with disproportionate pulmonary distribution of hepatic venous effluent. We studied the impact of total cavo-pulmonary connection (TCPC) geometry and the effect of increased cardiac output (CO) on distribution of inferior vena caval (IVC) return to the lungs.

Methods—10 Fontan patients – 5 with extra-cardiac (EC) and 5 with intra-cardiac (IC) configurations of the TCPC previously analyzed for power loss were processed for calculating the distribution of inferior vena caval return to the lungs (2nd order accuracy). One idealized TCPC was similarly analyzed under parametric variation of IVC offset and CO flow split.

Results—Streaming of the IVC return in the idealized TCPC model was dependent on both IVC offset magnitude and CO flow split ratio. For patient-specific TCPCs, preferential streaming of the IVC return was directly proportional to CO flow split ratio in the IC type TCPCs (p < 0.0001). Preferential streaming in EC TCPCs correlated to the IVC offset (p<0.05) and did not correlate to CO flow split. Enhanced mixing in IC is speculated to explain the contrasting results. Exercising tends to reduce streaming towards LPA in IC, while for EC, exercising tends to equalize the streaming.

Conclusions—EC and IC TCPCs have inherently different streaming characteristics due to contrasting mixing characteristics owing to their geometric differences. PA diameters and IVC offsets may together determine hepatic flow streaming.
Keywords
Arteriovenous malformation; pulmonary fistula; hepatic; Fontan

INTRODUCTION
Pulmonary arteriovenous malformations (PAVMs), also referred to as pulmonary arteriovenous fistulas (PAVFs) can occur after the Fontan procedure resulting in decreased systemic oxygenation. PAVMs are intrapulmonary arterial to venous shunts in which the systemic venous blood reaches the pulmonary venous system through abnormal vascular connections proximal to the gas exchange units. The primary consequence of PAVMs is decreased systemic oxygen saturation. The prognosis for Fontan patients with PAVMs is often poor without re-operation to reconstruct the Fontan baffle. PAVMs have been postulated in the past to be secondary to disproportionate distribution of hepatic factors between the two lungs. More recent studies confirmed that geometric configuration of the total cavopulmonary connection (TCPC) that preferentially stream hepatic vein (HV) flow to a single lung leads to PAVMs. Thus, it is important to determine TCPC geometric characteristics necessary to avoid preferential HV flow streaming. A recent study underscores the importance of geometric characteristics in a particularly complex case of PAVMs.

The TCPC is a double inlet double outlet connection that routes the venous return from the superior vena cava (SVC) and inferior vena cava (IVC) to the left pulmonary artery (LPA) and the right pulmonary artery (RPA). While most previous hemodynamic studies of the TCPC have focused on the power loss characteristics, flow streaming may be an equally important characteristic, specifically during the early growing period of the lung after conversion from Glenn stage to a Fontan. Thus one can postulate that an ideal TCPC needs to impose the least hemodynamic resistance (for minimal power losses) as well as facilitate balanced left and right streaming of inferior venous return for sufficient hepatic factor transport to both lungs.

In this study we quantify the flow branching of inferior blood returning via the Fontan baffle to the pulmonary arteries in the two major types of the TCPCs, namely extra-cardiac (EC) and intra-cardiac (IC) TCPCs. Of particular interest is the question: what are the geometric parameters of TCPC (e.g. PA diameters and vessel offset) that may be controlled during the construction of Fontan TCPC to avoid preferential streaming of HV flow? The answer to this question has strong clinical implications from the standpoint of choosing a particular TCPC type along with an understanding of the desired geometric characteristics for reducing the risk of PAVM formation. Also, it provides another perspective given the substantial literature on power loss characteristics of TCPC and its correlation with the geometry of the connection.

METHODS
The blood flow fields through 10 patient-specific TCPC geometries as well as an idealized TCPC geometry were computed using computational fluid dynamics tools and then analyzed to calculate the distribution of the IVC flow between the left and right lungs. The results were then examined to correlate TCPC geometry type (EC or IC) and influence of exercise on the distribution/streaming characteristics.
**Patient Data**

Ten patients, 5 each of EC and IC, were selected from the Georgia Tech MRI database of Fontan patients [http://fontan.bme.gatech.edu]. The database is part of an NIH-funded ongoing study for understanding Fontan hemodynamics. The demographics of the 10 patients are shown in Table 1. All patients were imaged at Children’s Hospital of Philadelphia (CHOP). Informed consent was obtained from all patients and all study protocols complied with the Institutional Review Boards of CHOP and the Georgia Institute of Technology. The inclusion criteria for this study were: (1) availability of axial MRI images to reconstruct the TCPC and aortic arch; (2) availability of clinical information necessary to categorize each study group; and (3) availability of computational results under resting and simulated exercise condition at equal pulmonary lung resistance condition. For all these criteria, 10 was the maximum out of over 200 patients in the database. For all 10 patients the anatomy of the TCPC was reconstructed using previously described segmentation and reconstruction techniques\(^\text{13-14}\). Geometric offset of the IVC relative to the SVC, were calculated for each of the patient specific TCPC from previously described methods\(^\text{15}\). There was no significant difference in cardiac output between the two groups of patients and the mean age of both groups was above the threshold\(^\text{16}\) for any variation in SVC/IVC flow ratio.

**Computational Model**

Computational fluid dynamics (CFD) simulations were conducted using FIDAP (ANSYS, Inc.) for each TCPC. Some of the data along with the detailed description of the simulation parameters has been published previously in the context of energy loss characteristics of the TCPC\(^\text{17}\). The flow conditions for each of the models correspond to the resting conditions and two simulated levels of exercise, namely the 2x and 3x resting flow condition\(^\text{17}\). The cardiac output (CO) flow split is defined as the fraction of the net inflow streaming to the LPA. In these simulations the CO flow split for each patient corresponds to imposed equal pulmonary lung resistance condition. Imposing this condition ensures that difference in the split of CO between the two lungs is purely governed by the resistance of the TCPC and not from differences in left and right pulmonary vascular bed resistances. This is an important condition to ensure that HV flow streaming characteristics are not biased by patient to patient variation in the difference between left and right lung resistance. To help develop an insight into the flow split physics, results on the idealized TCPC model are also presented for varying flow split and offset of the IVC from the SVC.

**Flow Split Computation**

Figure 1 shows a schematic that explains the methodology for flow split computation on an idealized 1D offset TCPC. 10,000 particles are uniformly seeded in a cross-section of the IVC. These particles have zero mass and their trajectories are computed by integrating the following equation using a 2\(^\text{nd}\) order runge-kutta numerical method:

\[
\begin{align*}
\dot{x} &= u(x, y, z) \\
\dot{y} &= v(x, y, z) \\
\dot{z} &= w(x, y, z)
\end{align*}
\]

Where \(u\), \(v\), and \(w\) are the three dimensional velocity components obtained from the computational model for each particle. Note that only the steady-state CFD solutions were considered for this analysis. Therefore, the velocity is not a function of time. \(\dot{x}\), \(\dot{y}\), and \(\dot{z}\) are the time-derivatives of the actual three dimensional particle position at time \(t\) given by \(x(t)\), \(y(t)\), and \(z(t)\).
Figure 2a shows a plot of all the trajectories calculated for the seeded particles in Figure 1. Each trajectory is sorted based on whether the particle is bound to the left lung or the right lung respectively. Based on the fate of the particle trajectory, the cross-section shown in Figure 1 is then partitioned into “left bound” or “right bound” areas. Examples of partitioning are shown in Figure 2b. The corresponding flow distribution is then calculated by integrating the velocity over the partitioned domains. Equations are shown at the two outlets of the LPA and RPA in Figure 1. The end result is the estimation of the exact split of the blood returning from the IVC to the two lungs. We note here that we assume the hepatic “factor(s)” to be uniformly mixed with the IVC blood. This calculation is denoted as HV flow split and is different from CO flow split in these sense that it is the split of IVC flow alone to the LPA.

Normalization

The CO flow split to LPA is normalized by CO and the estimated HV flow split to LPA is normalized to the total IVC flow. Therefore a 50% value indicates equal streaming.

Statistical Analysis—Since the data were non-normally distributed and corresponded to a two-sample population (EC vs IC), the non-parametric Mann-Whitney test was used to examine statistical significance among the various parameters evaluated. Differentiating factors are considered statistically significant for $p$ values $< 0.05$. Standard regression analysis is used to assess functional dependence where a $p$ value $< 0.05$ indicates a statistically significant functional dependence.

RESULTS

The results include calculation of the HV flow split for the idealized TCPC as well as the 10 patient-specific TCPCs. For the idealized TCPC, the HV flow split is calculated for varying offset between IVC and SVC (from 0.4D to D where the IVC is offset by one caval diameter (D) towards the RPA) and varying cardiac output split (i.e. percent cardiac output directed towards LPA). For the patient-specific TCPCs, HV flow split is calculated for the resting and two simulated exercise conditions (2x and 3x) all at equal pulmonary resistance condition.

Idealized TCPC

Figure 2a depicts the preferential streaming of inferior venous return to the right lung in a simplified 1-D offset model of the TCPC. The topological changes in the preferential streaming are further depicted in Figure 2b showing the cross section on the IVC where passive tracers were seeded color coded to right PA bound and left PA bound streams. These results show that the structure of the partitions change significantly with both the examined parameters, namely offset and CO flow split.

Patient-specific TCPCs

Shown in Figures 3 and 4 are the streaming details and normalized flow partitioning data obtained for the 5 IC and 5 EC TCPCs respectively. The patients are labeled by their database code (CHOPxxx). These results show that the flow partitioning structure from patient to patient is highly variable. Furthermore, the geometric structure of the partitioned cross-sections qualitatively remains similar between resting and simulated levels of exercise with only a gradual variation in HV flow split magnitude. Also subjectively, the geometric structure of partition for the IC has a finer scale (more convoluted, folded, often fractal like) than that for EC.
Figure 2 qualitatively showed a significant dependence of HV flow partitioning with CO flow split for the idealized TCPC. Figure 5 explores this dependence for the studied patient-specific cases. Note that due to imposed equal lung resistance conditions for the patient-specific TCPCs, any variations observed in the CO flow split are purely due to the directional resistance and geometric properties of the patient-specific TCPCs. Data points for both rest and simulated exercise conditions have been plotted in Figure 5. From this figure it is clear that IC TCPCs have a near linear correlation with \( p < 0.0001 \) and \( R^2 = 0.93 \) between HV flow split and CO flow split. The slope and intercept of the linear relationship are: 0.84 (±0.07) and 15.02% (±3.30) respectively. Quantities in the brackets correspond to standard error. No significant correlation was found for the EC TCPCs. Figure 6 investigates the effect of IVC offset in EC TCPCs. A significant correlation existed with decrease in LPA streaming with increasing IVC offset towards the RPA (\( p<0.01 \) and \( R^2 > 0.91 \)). The slope of the correlation did not significantly change with exercise.

Figure 7 illustrates the effect of exercise on the streaming characteristics. No statistically significant trends could be detected. However it appears that increase in cardiac output mildly reduced LPA streaming in intra-cardiacs while for extra-cardiacs exercising tended to eliminate streaming by approaching the valve of 50–50 asymptotically.

**DISCUSSION**

This study, to the best of our knowledge, is the first that analyzes HV flow streaming to the lungs with respect to geometric characteristics of the TCPC, and examines any influence exercising may have on HV streaming. The problem is highly relevant as surgeons have the opportunity during the construction of the TCPC to ensure adequate distribution of HV flow to both the lungs as well as to minimize any hemodynamic energy losses. Failure to construct an optimal TCPC may result in the need for Fontan revision in which the palliative strategy for correction of PAVMs typically involves attempts to redirect the hepatic effluent to the affected lung. Several approaches have been proposed to accomplish this objective including a transcatheter reconnection\(^{18}\), formation of arteriovenous fistulae\(^{19}\), rerouting of the hepatic venous flow to the hemiazygos vein\(^4\), \(^{20}\), redirection of the hepatic venous flow to the innominate vein\(^{21}\), and the use of a bifurcated extracardiac conduit\(^{22}\), to name a few. Clearly, the wide variety of patient anatomies makes it difficult to design a general procedure that will suit all patients. Additionally, the complexity of patient anatomies poses significant challenges to identify the surgical option that will best distribute hepatic flow for a given patient. Below we discuss the above presented results and focus on the following two objectives of this study: (1) Influence of TCPC Geometry and CO Flow split, and (2) Influence of Exercising.

**Influence of TCPC Geometry and CO Flow split on HV Flow Streaming**

It is clear from the results that both geometry and CO flow split play a crucial role on HV flow streaming. Intuitively, this is obvious. Any change in geometric conditions or flow conditions is bound to change the flow field and hence impact how streams of hepatic factors interact with the SVC flow. These interactions include mixing as well as “splitting” into left bound and right bound flow.

For the idealized TCPC, we studied the geometric change corresponding to the IVC offset and the CO flow split as independent parameters (see Figure 2). As expected, both these parameters changed the partitioning (shown in Figure 2b). These results can be explained as follows: The tendency of the IVC flow to stream preferentially to the RPA is due to the “momentum barrier” created by the opposing SVC flow. In other words, the IVC flow needs to cross the SVC stream to reach the LPA side. Therefore the more the IVC is offset, the more difficult it is for HV flow to overcome the barrier and stream to the LPA. This effect is
amplified when the CO preferentially splits to the RPA. Therefore for the idealized TCPC, both the independent parameters made a significant influence on the HV flow streaming. The results for the patient-specific TCPCs as described below are more interesting and are quantitatively analyzed.

Figure 5 clearly shows a drastic difference between IC and EC streaming characteristics. Specifically, preferential streaming in IC is directly proportional to the CO flow split as depicted by the linear relationship. In contrast EC TCPCs did not significantly depend on the CO flow split. This is an interesting observation and the fluid dynamic explanation is that it may be attributed to “mixing” between the SVC and IVC streams, which is higher in IC and lower in EC. The fact that there is more mixing in IC compared to EC is evidenced by the presence of “finer scale” structures in the partitions shown in Figure 3 compared to those shown in Figure 4. Notice the presence of structures resembling a “stirring” effect (analogous to the mixing of creamer when poured in black coffee). Qualitatively, these structures resembling mixing are much reduced in EC TCPCs in Figure 4. Theoretically, if the SVC and IVC streams perfectly mix, then the HV flow split would be exactly equal to the CO flow split. Based on this observation, it may be presumed that any streaming tendencies in IC TCPCs are governed by the CO flow split which in turn is known to be related to the directional resistance of the TCPC.

From our previous studies it is known that both CO and the CO split are primarily correlated to the PA diameters. Therefore a corollary is that for the IC TCPCs, streaming is proportional to the PA diameter. In other words, more hepatic factors will go to the bigger PA.

Given that there is no significant mixing in EC TCPCs, the streaming is more sensitive to the relative orientation between the IVC and the SVC. As shown in Figure 6, the HV flow streaming characteristics of EC TCPCs primarily depend on the IVC offset. Notice that as the IVC offset increases, HV flow streaming toward LPA decreases. This is also consistent with the results shown in Figure 2 for an idealized EC TCPC model. The fluid dynamic explanation is the same as that given for the idealized TCPC. The SVC flow creates a momentum barrier for the flow from the IVC to cross to reach the LPA side. As confirmed from Figure 6, increase in offset reduces the net hepatic factors streamed towards the left lung. Figure 6 also shows that exercising does not appear to alleviate preferential streaming in ECs. This is supported by the observation that the slope of the linear regression lines between the resting and the simulated exercise conditions were not statistically different. These results combined with previous studies on power loss characteristics show that for the EC TCPCs, offsetting the IVC is a tradeoff problem between power loss and HV streaming.

Influence of Exercise on HV Flow Streaming

Exercising is an important factor when it comes to the power loss characteristics of the TCPC. However, the present study shows that exercise has only a marginal effect on HV streaming characteristics with no statistical significance as seen in Figure 7. At best, it appears that exercising has the following slight influence on streaming: For IC TCPCs, exercise always reduces the streaming to LPA. This may be related to the fact that the LPA is often a little smaller than the RPA thus shifting the CO flow split towards the RPA. For EC TCPCs exercise always appears to equalize the streaming, and this may be due to enhanced mixing from higher flow instabilities and turbulence at higher flow rates.

A note on SVC flow streaming

While the above results and discussion are provided in the context of preferential IVC flow streaming, they are also applicable to SVC flow streaming (based on the symmetry of the
An explicit relationship between SVC flow streaming and IVC flow streaming can be derived using the principle of conservation of mass. Let $\alpha$ denote IVC flow split to LPA, $\beta$ denote SVC flow split to LPA, $\gamma$ denote the ratio of IVC flow to SVC flow, and $\delta$ denote CO flow split to LPA. Then conservation of mass principle (net mass inflow = net mass outflow) requires the following equation to hold:

$$\beta = \delta - \gamma(\alpha - \delta)$$

In words, the SVC flow split will be lower than the CO flow split by an amount proportional to how much IVC flow split is greater than CO flow split. The proportionality is equal to $\gamma$, the ratio between the IVC flow and SVC flow. If IVC and SVC flows are equal then the equation simplifies to $\beta = 2\delta - \alpha$.

**CONCLUSION AND CLINICAL SIGNIFICANCE**

In conclusion, while the idealized TCPC study showed that both offset and CO split play a significant role on the HV streaming, the relative contributions of these independent factors were different between IC and EC patient-specific TCPCs. Specifically, HV streaming in EC TCPCs primarily depends on the IVC offset; CO split primarily governs the HV streaming in IC TCPCs. More mixing between the SVC and IVC streams in IC TCPCs could be the cause for the contrasting HV streaming characteristics between IC and ECs. Clinically these results translate to optimizing two parameters, namely PA diameters and the IVC offset in the case of EC TCPC contraction. Ensuring that the PA sizes are nearly equal without stenosis can ensure a well-balanced CO flow split. This is beneficial from both energy loss standpoint as well as HV flow streaming. The optimization of IVC offset for EC construction is a trade-off situation. While increasing the IVC offset can have benefits from energy loss standpoint, it may be non-beneficial from a HV streaming standpoint. While the above guidelines may not directly influence the conversion from 2nd stage to the Fontan connection, they may help in cases related to reconstruction or repair of a Fontan in patients with complications secondary to poor HV effluent distribution.

**Acknowledgments**

The authors gratefully acknowledge the Bioengineering Research Partnership (BRP) grant from NIH (HL67622). Dr. Whitehead was supported in part by the NIH training grant T32 HL007915-08.

**References**


J Thorac Cardiovasc Surg. Author manuscript; available in PMC 2012 January 1.


Figure 1.
Mathematical definition of inferior venous split to the two pulmonary arteries depicted on a simplified 1-D offset idealization of the TCPC. 100,000 mass-less particles denoted as set \( \{P_i\} \) are seeded in the IVC and tracked using the velocity field output of the computational model. The seeding cross-section is then partitioned into \( \Omega_{LPA} \) and \( \Omega_{RPA} \) based on the fate of the particle after it transits through the connection.
Figure 2.
Visualization of streamlines (A) color coded (red stands flow bound to the left lung; blue stands for flow bound to the right lung) on the 1-D offset model; and (B) partitioning the seeding cross-section of the IVC (shown in Figure 1) to left and right bound flow distribution for varying CO flow split and the variation of offset.
Figure 3.
The five patient-specific IC TCPCs depicting flow streaming at resting conditions (top row). Also shown for each patient is the color-coded partitioning at the particle seeding cross-section of the IVC as a function of simulated exercise level. Blue represents Left bound and red represents right bound flow.
Figure 4.
The five patient-specific EC TCPCs depicting flow streaming at resting conditions (top row). Also shown for each patient is the partitioning at the particle seeding cross-section of the IVC as a function of simulated exercise level. Blue represents Left bound and red represents right bound flow.

<table>
<thead>
<tr>
<th>CHOP055</th>
<th>CHOP067</th>
<th>CHOP088</th>
<th>CHOP089</th>
<th>CHOP090</th>
</tr>
</thead>
<tbody>
<tr>
<td>Streams</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>x1</td>
<td>64.15</td>
<td>35.85</td>
<td>32.50</td>
<td>67.50</td>
</tr>
<tr>
<td>Partitioning x2</td>
<td>58.59</td>
<td>41.41</td>
<td>32.32</td>
<td>67.68</td>
</tr>
<tr>
<td>x3</td>
<td>57.26</td>
<td>42.74</td>
<td>34.75</td>
<td>65.25</td>
</tr>
</tbody>
</table>
Figure 5.
IVC to LPA streaming as a function of fraction of CO to LPA for all 10 patients at resting and simulated conditions (connected symbols). IC patients showed a significant linear correlation $p < 0.0001$ and $R^2 = 0.93$ (dashed line) while EC patients did not show significance $p > 0.05$. 
Figure 6.
LPA streaming as a function of IVC Offset towards RPA in EC TCPCs. Offset is normalized to IVC diameter. Linear regression gives $R^2 > 0.91$ and $p < 0.01$ for each of the fitted lines. The slight decrease in slope with increasing cardiac output was not statistically significant.
Figure 7.
Effect of exercise on LPA streaming characteristics of IC and EC TCPCs shown separately. For IC the overall streaming decreases marginally with exercise. For EC streaming appears to tend to a value of 50% streaming with exercise.
Table 1
Summary of differences in demographics and cardiac output for the EC and IC geometries. Table is modified from: Circulation 2007; 116: II_481.

<table>
<thead>
<tr>
<th></th>
<th>All</th>
<th>EC</th>
<th>IC</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (Y)</td>
<td>10.2 ± 4.7</td>
<td>6.6 ± 2.2</td>
<td>13.2 ± 3.7</td>
<td>&lt; 0.01</td>
</tr>
<tr>
<td>BSA (m²)</td>
<td>1.14 ± 0.4</td>
<td>0.78 ± 0.2</td>
<td>1.4 ± 0.28</td>
<td>&lt; 0.01</td>
</tr>
<tr>
<td>CO (L/min)</td>
<td>2.9 ± 1.0</td>
<td>2.6 ± 1.1</td>
<td>3.4 ± 0.7</td>
<td>0.17</td>
</tr>
<tr>
<td>CI (L/min/m²)</td>
<td>2.7 ± 0.4</td>
<td>2.9 ± 0.4</td>
<td>2.5 ± 0.3</td>
<td>0.11</td>
</tr>
<tr>
<td>SRV</td>
<td>4</td>
<td>1</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>SLV</td>
<td>6</td>
<td>4</td>
<td>2</td>
<td></td>
</tr>
</tbody>
</table>

Abbreviations: Body surface area (BSA); Cardiac output (CO), Cardiac Index (CI), Single Right Ventricle (SRV), Single Left Ventricle (SLV).