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Michal Schäfer, MD, PhD, Michael V. Di Maria, MD, James Jaggers, MD, Matthew L. Stone, MD, PhD, David N. Campbell, MD, D. Dunbar Ivy, MD, Max B. Mitchell, MD

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Hemi-Fontan and Bi-directional Glenn operations Result in Flow Mediated Viscous Energy Loss at the time of Stage II Palliation

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Michal Schäfer, MD, PhD;¹ Michael V. Di Maria, MD;² James Jaggers, MD;¹ Matthew L. Stone, MD, PhD;¹ David N. Campbell, MD;¹ D. Dunbar Ivy, MD;² and Max B. Mitchell, MD;¹

1. Division of Cardiothoracic Surgery, University of Colorado Denver | Anschutz Medical Campus, Aurora, CO
2. Division of Pediatric Cardiology, Children’s Hospital Colorado, University of Colorado Denver | Anschutz Medical Campus, Aurora, CO

Address for correspondence:
Michal Schäfer
Heart Institute
Children’s Hospital Colorado
13123 E 16th Ave
Aurora, CO 80045-2560
(720) 777-2940
Fax: (720) 777-7290
michal.schafer@cuanschutz.edu

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Glossary of Abbreviations:

4D-Flow MRI = four dimensional flow magnetic resonance imaging
BDG = bi-directional Glenn

$E_L$ = viscous energy loss
HF = hemi-Fontan
HLHS = hypoplastic left heart syndrome
SCPC = superior cavo-pulmonary connection
SVC = superior vena cava

**Key words:** hemi-Fontan, bi-directional Glenn, flow hemodynamics

**Central Picture**
Comparison of HF and BDG flow hemodynamic patterns.

**Central Message**
The second stage of surgical palliation of HLHS using either HF or BDG results in similar flow mediated viscous energy loss throughout the SCPC junction.

**Perspective Statement**
4D-Flow MRI results compliment previous computational results suggesting minimal differences in mechanical fluid dissipating energy loss, particularly in the context of the entire pulmonary circuit. 4D-Flow MRI and computational methods should be applied together to investigate flow hemodynamic patterns throughout the Fontan palliation.
ABSTRACT

Objective: Superior cavo-pulmonary connection (SCPC) for Stage II palliation most commonly is achieved by either the bidirectional Glenn (BDG) or hemi-Fontan (HF) operations. The comparison of flow hemodynamic efficiency at the region of surgical reconstruction and in proximal pulmonary arteries has been primarily evaluated using computational modeling techniques with conflicting reports. Thus, the purpose of this descriptive study was to compare flow hemodynamics following Stage II (BDG vs. HF) using 4D-Flow MRI with particular focus on flow mediated viscous energy loss ($E_L$) under matched hemodynamic conditions.

Methods: Patients with HLHS who underwent either HF or BDG as part of the Stage II palliation underwent pre-Fontan 4D-Flow MRI. Patients were matched by the pulmonary vascular resistance index, net superior vena cava (SVC) flow, right and left pulmonary artery (RPA and LPA) size, and age. Maximum $E_L$ throughout the cardiac cycle was calculated along the SVC-RPA and SVC-LPA tract.

Results: 8 patients who underwent HF as part of their Stage II single ventricle palliation were matched with 8 patients who underwent BDG. There were no differences in median volumetric indices including end-diastolic ($P = 0.278$) and end-systolic volumes ($P = 0.213$). No differences were further observed in ejection fraction ($P = 0.091$) and cardiac index ($P = 0.324$). There were no differences in measures peak $E_L$ measured along the SVC-RPA tract (median HF: 0.05 vs 0.04 mW, $P = 0.365$) and SVC-LPA tract (median: 0.05 vs 0.04 mW, $P = 0.741$).

Conclusion: The second stage of surgical palliation of HLHS using either HF or BDG results in similar flow mediated viscous energy loss throughout the SCPC junction. 4D-Flow MRI and computational methods should be applied together to investigate flow hemodynamic patterns throughout the Fontan palliation and overall efficiency of the Fontan circuit.
INTRODUCTION

Stage II surgical palliation for hypoplastic left heart syndrome (HLHS) by superior cavo-pulmonary connection results in non-pulsatile flow from the superior vena cava (SVC) to the pulmonary arteries independent of ventricular support. The aim of surgical reconstruction, therefore, is to yield a system with minimal pressure and energy loss in the proximal pulmonary arteries\(^1\). Superior cavo-pulmonary connection (SCPC) for Stage II palliation most commonly is achieved by either the bidirectional Glenn (BDG) or hemi-Fontan (HF) operations. While the BDG operation creates a communication between the SVC and undivided pulmonary arteries, the HF procedure augments the pulmonary artery without dividing SVC and excludes flow from the inferior cava by means of a temporary atrial patch\(^2,3\). The majority of studies evaluating pulmonary circulation in patients with single ventricle physiology are focused on hemodynamic state post completed palliation\(^4,5\). However, direct comparison of the flow hemodynamic state between the operative techniques at the intermediate stage II using \textit{in-vivo} flow imaging has not yet been done.

The comparison of flow hemodynamic efficiency at the region of surgical reconstruction and in proximal pulmonary arteries has been primarily evaluated using computational modeling\(^6\). Computational studies have reported conflicting results on fluid energy dissipation loss through the SCPC and proximal pulmonary arteries likely given to different methodological approaches\(^7-9\). In contrast to computational methods, 4D-Flow MRI directly measures velocity and does not rely on assumptions about physiologic boundary conditions such as vascular compliance and resistance; however, it lacks spatiotemporal resolution\(^10\). Lately, interrogation of the Fontan circulation has been shown feasible using 4D-Flow MRI flow mediated viscous
energy loss ($E_L$)\textsuperscript{11–13}. Unlike hydraulic or mechanical fluid energy loss, $E_L$ is a form of frictional energy loss due to viscous interaction within the fluid domain and indirectly measures the amount of flow inefficiency due to secondary flow characteristics such as vortices or helices\textsuperscript{14}.

Thus, the purpose of this descriptive study was to compare flow hemodynamics following Stage II (BDG vs. HF) using 4D-Flow MRI with particular focus on flow mediated $E_L$ under matched hemodynamic conditions. We present the results of this series to propose an additional flow hemodynamic parameter to complement previous computational studies concerning the interstage phase of the Fontan palliation.

METHODS

This descriptive study was a part of larger prospective study investigating flow hemodynamic conditions in children with congenital heart disease using cardiac MRI and 4D-Flow MRI approved by Colorado Multi-institutional Review Board with waived written consent (#19-1420; date of approval: June 20, 2019). Cardiac MRI including 4D-Flow MRI at our is currently part of standard pre-Fontan evaluation in addition to echocardiographic and catheterization evaluations. All included patients in this series had history of HLHS palliated initially by Norwood procedure and followed by either HF or BDG. Patients were pair-wise matched by physiologic, geometric, and demographic parameters including pulmonary vascular resistance index, net superior vena cava flow, size of branch pulmonary arteries, and age of MRI acquisition. Patients with significant stenotic lesion treated with stent or balloon angioplasty were not included. Waiver of informed consent within the study population was approved, and all procedures were in accordance with the principles outlined in the Declaration of Helsinki.
Cardiac MRI Protocol

All patients underwent standardized CMR evaluation previously described institutional protocol with prescribed sequences customized for single ventricle evaluation\(^{15}\). 3.0 T system (Ingenia, Philips Medical Systems, Best, The Netherlands) was applied to acquire balanced steady-state free precession stacks of short-axis images covering the ventricles from base to apex. Long-axis and 4-chamber views were obtained in each subject with plane orientations detailed to appreciate the atrio-ventricular valves and outflow tracts. Lastly, trough plane views of the SCPC and proximal pulmonary arteries were obtained.

4D-Flow MRI protocol was conducted as shown previously\(^{16}\). Briefly 4D-Flow MRI sequence was acquired in a sagittal plane with typical sequence parameters as follows: echocardiograph times = 2.4 to 2.6 msec, repetition times = 4.2 to 5.0 msec, flip angle = 10°, temporal resolution = 42 to 50 msec, field of view: 250 × 320 or 200 × 250 mm\(^2\), 14 to 18 cardiac phases, voxel size = 2.0-2.4 × 2.0-2.4 × 2.2-2.6 mm\(^3\), velocity encoding = 100 to 150 cm/s, and acquisition time = 10 to 15 minutes depending on respiratory gating efficiency.

Viscous Energy Loss Calculation

Power loss refers to the mechanical fluid energy dissipation loss when blood is moved along the vasculature. This is primarily determined by the pressure differences and this “hydraulic” power loss has been preferentially investigated in computational fluid dynamic studies. In real conditions, there are also additional mechanical energy losses due to friction, and those could be due to viscous (\(E_{L}\)) or turbulent energy losses. \(E_{L}\) is inversely related to vessel radius and is the main cause of energy loss in stationary laminar flow which closely resembles
Fontan circulation. $E_L$ could further increased if the flow through a vessel is not laminar and cohesive and creates secondary flow formations such vortices or helices.

Flow mediated viscous energy loss $E_L$ was calculated in each patient along the predefined vascular tracked as proposed previously $^{17}$ (Figure 1). All post-processing components were done using commercially available post-processing platform (Circle CVI42, Calgary, Canada). Anatomical structures were identified from 4D-flow MRI–derived magnetic resonance angiography which served for subsequent structural segmentation. Segmented contours of the superior vena cava, SCPC, and pulmonary arteries served for the regional delineation and definition of the centerline along which was $E_L$ calculated. The first path included segment from the superior vena cava (SVC) starting at the junction of innominate veins and followed a centerline through SCPC and approximately 2 cm to right pulmonary artery. The second path started at the same location at the innominate vein junction and followed a centerline to the left pulmonary artery. Peak $E_L$ encountered throughout the cardiac cycle was recorded for each patient and adjusted for a total centerline length. The determination of instantaneous viscous energy loss due to frictional forces is calculated per individual voxel within a predefined segmented region and yields units of power loss in milliWatts (mW).

Statistical Analysis

This was primarily a descriptive study, and collected demographic and hemodynamic values were reported as mean ± standard deviation or median with corresponding interquartile range as dictated by the dataset distribution. Pair-wise matching was based on parameters directly influencing $E_L$ including flow rate (net flow through SVC) and diameter of pulmonary arteries, as well as by physiologic and demographic parameters including pulmonary vascular
resistance index, age of MRI acquisition, and age at Stage II operation. Patients were matched 1:1 based on propensity score matching. The probability of undergoing HF versus BDG was calculated by a multivariable logistic regression model that contained pulmonary vascular resistance index, net superior vena cava flow, size of branch pulmonary arteries, and age of MRI acquisition. Comparative analysis of flow hemodynamic parameters between HF and BDG patients was obtained using Wilcoxon paired match test. All statistical analyses and data presentation were performed with Prism (version 9.5.1; GraphPad Software Inc) and Gardner-Altman figures were generated using Estimation Plots. All performed tests were 2-sided and significance was based on an alpha-level of $\leq 0.05$.

RESULTS

In total 8 patients who underwent HF as part of their Stage II single ventricle palliation were matched with 8 patients who underwent BDG. Patients’ demographics and hemodynamics are reported in Table 1. Specific diagnoses included HLHS with aortic atresia / mitral stenosis (N = 6), aortic atresia / mitral atresia (N = 4), aortic stenosis / mitral stenosis (N = 6). All patients underwent Norwood procedure as part of their initial palliation with right-ventricular to pulmonary artery shunt (N=9) or modified Blalock-Taussig shunt (N = 7). Median age at the time of Stage II operation was for both patient groups 5 months and similarly median age at the time current MRI scan was 2.5 years for both HF and BDG groups. There were no differences in pre-Fontan pulmonary vascular resistance index (HF: 1.9 vs BDG: 2.1 WU, $P = 0.641$). No differences were observed in median net SVC flow or branch pulmonary artery diameters and they respective $z$-scores. No patient had worse than mild-to-moderate tricuspid regurgitation per
the same day echocardiography. Presently, all patients successfully underwent Fontan procedure without major complications requiring further re-operation.

Cardiac MRI hemodynamics are summarized in **Table 2**. There were no differences in median volumetric indices including end-diastolic (median HF: 130 vs BDG: 105 mL/m², \( P = 0.278 \)) and end-systolic volumes (median HF: 71 vs BDG: 50 mL/m², \( P = 0.213 \)). No differences were further observed in ejection fraction (median HF: 48 vs BDG: 50 %, \( P = 0.091 \)), cardiac index (median HF: 4.7 vs. 5.5 L/min/m², \( P = 0.324 \)), aorto-pulmonary collateral flow burden (median HF: 34 vs BDG: 46 %, \( P = 0.275 \)).

Comparison of the 4D-Flow MRI derived \( E_l' \) is graphically depicted using Gardner-Altman plots in **Figure 2** and in **Table 2**. There were no differences in measures peak \( E_l' \) measured along the SVC-RPA tract (median HF: 0.05 vs 0.04 mW, \( P = 0.365 \)) and SVC-LPA tract (median: 0.05 vs 0.04 mW, \( P = 0.741 \)). Qualitatively, flow patterns were distinctively different between HF and BDG patients (**Figure 3**). In patients with HF configuration, flow through the SVC is projected to respective pulmonary arteries already at the level of floor of the patch dividing the SVC. Portion of the flow directed to RPA typically creates a secondary flow formation in a form of helical form observed in 5 (63%) of the HF patients. This flow pattern appears to result from an incoming flow trajectory when pathlines collide with the posterior wall of the pulmonary artery and re-bounce again on the posterior aspect of the SVC or pulmonary artery giving a rise to helical formation (**Figure 4**). This helical flow pattern was absent in left pulmonary artery in all HF patients.

In contrast to HF patients, BDG configuration resulted in all cases into cohesive uniform flow without any secondary flow formations proximal or distal to the SCPC region. The flow through the SVC typically splits directly at the level of SVC pulmonary artery junction with
further redirection dictated by the geometric orientation of pulmonary arteries without any
vortical or helical formations.

DISCUSSION

In this descriptive study we report comprehensive qualitative and quantitative flow
hemodynamic indices in patients who underwent either HF or BDG as the second part of their
surgical palliation for HLHS. The primary findings of this report are as follows: 1) there are no
quantitative differences between both procedures in flow patterns as evaluated by $E_L$ with minor
qualitative flow differences in RPA and 2) there were no differences in standard pre-Fontan
cardiac MRI hemodynamics. These findings are further highlighted by similar physiologic and
geometric conditions in both patient groups. Our results supplement findings from previous
computational studies with direct in-vivo 4D-Flow MRI measurements and suggest the feasibility
of flow hemodynamic mapping prior to completion of the Fontan palliation.

To the best of our knowledge, all previous studies comparing flow hemodynamic
efficiency of the SCPC using either the HF or BDG surgical approach has been done using
computational simulations with variable outcomes\textsuperscript{8,9,19,20}. Variable study designs and approaches
defining the geometric boundary conditions using different imaging modalities with physiologic
inputs derived from catheterization or phase-contrast MRI are a likely cause for the minor
discrepancies in observed results. The earliest comparative study utilizing computational fluid
dynamics (CFD) by Bove et al investigated hydraulic power loss\textsuperscript{9}. The authors observed no
differences at Stage II but reported higher energy losses in patients who underwent BDG after
the completion of Fontan procedures. A subsequent study by Pekkan et al found that the BDG
connection is hemodynamically more efficient when compared to HF using stereolithographic
models of patient specific anatomies in combination with phase-contrast MRI data serving as the flow input\textsuperscript{8}. A recent study by Kung et al applied multiscale modeling approach using the same patient pre-operative anatomies and virtually superimposed either the HF or BDG template on the final hemodynamic system\textsuperscript{20}. The authors observed highly variable energy losses at the level of SCPC junction between both techniques with slightly worse hydraulic energy loss in some HF patients; critically, they also reported that the local power losses have negligible effects on the entire pulmonary circulation and final physiologic and hemodynamic outcomes were same for both groups.

It is important to consider measured flow mediated energy loss in the context of the entire pulmonary circuit and single ventricular power. The majority of studies report on local energy loss in the range of 0.1 to 3.5 mW. Studies modeling HF surgical configuration showed that total mechanical power loss across the entire pulmonary bed can reach over 15 mW, and consequently local flow mediated energy dissipation was calculated to represent 1 to 16\% of the overall energy loss and less than 2\% of ventricular power loss\textsuperscript{20,21}. However, this energy loss can be more severe in the setting of proximal pulmonary arterial stenosis and might be more profound during exercise\textsuperscript{22}. In patients with the BDG configuration, a highly uneven flow ratio to the branch pulmonary arteries has been shown to increase flow energy loss with the minimal energy loss achieved at near normal physiologic 55\% split flow to the right pulmonary artery\textsuperscript{23}. Additional consideration should be paid to the shear dependent blood viscosity otherwise known as non-Newtonian behavior, describing a non-linear relationship between shear stress and shear strain at low velocity venous flow conditions. A study by Cheng et al showed that considering this physiologic property significantly alters flow hemodynamic outcomes including power loss,
pulmonary flow distribution, shear stress, and caval flow mixing in Fontan circulation; yet this property is often omitted in computational studies\(^24\).

Our data showed that flow mediated viscous energy loss \(E_L\) in pre-Fontan stage ranges between 0.02 to 0.10 mW, which is approximately one third lower than values reported in studies evaluating the completed total cavo-pulmonary anastomosis\(^25,26\). Based on our results and previously discussed computational studies, we believe that \(E_L\) and quality of flow formations represents only a minimal role in the overall mechanical energy loss in the pulmonary circuit, particularly in circuits with significant stenoses. However, \(E_L\) represents only mechanical energy loss due to frictional losses and the overall hydraulic energy loss is therefore underestimated.

Furthermore, while 4D-Flow MRI derived \(E_L\) measurements are considered reliable in comparative studies\(^27\), they typically underestimate the true \(E_L\) as shown by computational studies\(^28\). Qualitatively, observed helical flow through the right pulmonary artery in HF did not significantly increase \(E_L\). We speculate that this is primarily due to a low velocity flow system and relatively short distance along which the \(E_L\) was measured. Also, the role of helical flow through large vessels needs to be further explored as higher helicity has been previously associated with better hemodynamic outcomes in patients with pulmonary hypertension\(^29,30\).

Future studies using 4D-Flow MRI estimated \(E_L\) should be evaluated in the context of stress exercise using MRI compatible devices to appreciate the energy loss in the context of higher myocardial workload.

Limitations

This was an early-stage descriptive study considering only patients without significant stenoses with favorable pre-Fontan stage hemodynamics, resulting in a significant patient
selection bias. Furthermore, this was only a single center study reflective of surgical techniques at our institution. At this time, we also did not have post-Fontan stage flow hemodynamic parameters for a final outcome comparison of the two techniques. Additional limitations are primarily pertinent to the 4D-Flow MRI technique, including limited spatiotemporal resolution and inability to study flow hemodynamic patterns in patients with implanted stents. We believe that multimodality studies involving both 4D-Flow MRI and CFD would be highly beneficial in investigating flow hemodynamic patterns and their overall role during the interstage phase of the Fontan palliation and in long-term clinical outcomes.

CONCLUSION

The second stage of surgical palliation of HLHS using either HF or BDG results in similar flow mediated viscous energy loss throughout the SCPC junction. Our 4D-Flow MRI results compliment previous computational results suggesting minimal differences in mechanical fluid dissipating energy loss, particularly in the context of the entire pulmonary circuit. 4D-Flow MRI and computational methods should be applied together to investigate flow hemodynamic patterns throughout the Fontan palliation and to investigate the role of flow mediated energy loss in predicting clinical outcomes and overall efficiency of the Fontan circuit.

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### TABLES

**Table 1. Patient characteristics and hemodynamics**

<table>
<thead>
<tr>
<th></th>
<th>Hemi-Fontan (N = 8)</th>
<th>Bi-Directional Glenn (N =8)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age at MRI (years)</td>
<td>2.5 (2.0 - 3.1)</td>
<td>2.5 (2.0 - 3.0)</td>
<td>0.641</td>
</tr>
<tr>
<td>Sex (Female)</td>
<td>3 (38%)</td>
<td>3 (38%)</td>
<td>-</td>
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<tr>
<td>BSA (m²)</td>
<td>0.61 (0.56 – 0.63)</td>
<td>0.59 (0.56 – 0.63)</td>
<td>0.766</td>
</tr>
<tr>
<td>Age at Stage II (months)</td>
<td>5 (4 - 6)</td>
<td>5 (4 - 6)</td>
<td>0.925</td>
</tr>
</tbody>
</table>
Table 2. Patient characteristics and hemodynamics

<table>
<thead>
<tr>
<th></th>
<th>Hemi-Fontan (N = 8)</th>
<th>Bi-Directional Glenn (N = 8)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>End-diastolic volume index (L/m²)</td>
<td>130 (11 – 160)</td>
<td>105 (103 – 111)</td>
<td>0.278</td>
</tr>
<tr>
<td>End-systolic volume index (L/m²)</td>
<td>71 (54 – 83)</td>
<td>50 (45 – 56)</td>
<td>0.213</td>
</tr>
<tr>
<td>Stroke volume index (L/m²)</td>
<td>61 (56 – 62)</td>
<td>53 (50 – 63)</td>
<td>0.954</td>
</tr>
<tr>
<td>Ejection fraction (%)</td>
<td>48 (42 – 51)</td>
<td>50 (48 – 56)</td>
<td>0.091</td>
</tr>
<tr>
<td>Cardiac index (L/min/m²)</td>
<td>4.7 (4.2 – 5.0)</td>
<td>5.5 (5.1 – 6.1)</td>
<td>0.324</td>
</tr>
<tr>
<td>AP-collateral flow %</td>
<td>34 (29 – 38)</td>
<td>46 (34 – 50)</td>
<td>0.275</td>
</tr>
<tr>
<td>SVC – RPA $E_L$ (mW)</td>
<td>0.05 (0.03 - 0.07)</td>
<td>0.04 (0.03 - 0.06)</td>
<td>0.365</td>
</tr>
<tr>
<td>SVC - LPA $E_L$ (mW)</td>
<td>0.05 (0.03 - 0.07)</td>
<td>0.04 (0.03 - 0.10)</td>
<td>0.741</td>
</tr>
</tbody>
</table>

Data reported as median with corresponding IQR. Reported P-values represent paired Wilcoxon matched pair rank tests. SVC = superior vena cava, PVRi = pulmonary vascular resistance index, WU = Wood’s unit, RPA = right pulmonary artery, LPA = left pulmonary artery, $E_L$ = viscous energy loss.
used to segment the superior vena cava (SVC) and right and left pulmonary arteries (RPA and LPA). C) Viscous energy loss was then calculated along the SVC-RPA and SVC-LPA tracts.

**Figure 2.** Graphical depiction of the comparative analysis of viscous energy loss between hemi-Fontan and bi-directional (BDG) techniques along the SVC-RPA A) and SVC-LPA B) paths.

**Figure 3.** Representative comparison of the hemi-Fontan A) and bi-directional Glenn B) 4D-Flow MRI cases and corresponding viscous energy loss heat maps along the superior vena cava to branch pulmonary arteries. White arrows indicate a predominant pathline trajectory to respective branch pulmonary arteries. A minor helical formation can be noticed from the lateral view in the right pulmonary artery of the patient who underwent hemi-Fontan procedure. This helix was noticed in 5/8 HF cases and was absent in all bi-directional Glenn subjects.

**Figure 4.** Temporal evolution of flow in the representative hemi-Fontan configuration throughout the cardiac cycle A-I). There were no secondary flow formation observed in the area of cavo-atrial junction but small helix in the right pulmonary artery can be appreciated in mid-systolic phase.