Patient-specific hemodynamic performance of Fontan conversion templates: *Lateral tunnel vs. intra-atrial with fenestration*

Haifa Hong[1], Onur Dur[2], Haibo Zhang[1], Zhongqun Zhu[1],

Huiwen Chen[1], Kerem Pekkan[2], Jinfen Liu[1]

(1) The Cardiothoracic Surgery Department, Shanghai Children's Medical Center, Medical School Shanghai Jiaotong University, Shanghai, China

(2) Biomedical Engineering Department, Carnegie Mellon University, Pittsburgh, PA

Running title: Pulsatile performance of lateral tunnel and intra-atrial connections

Authors for Correspondence:

Jinfen Liu, Department of Cardiac and Thoracic Surgery, Shanghai Children's Medical Center, Xinhua Hospital, Shanghai Jiaotong University School of Medicine, 1678 Dongfang Road, Shanghai 200127, China (e-mail address: paulliujinfen@gmail.com); Kerem Pekkan, Biomedical Engineering Department, Carnegie Mellon University, Pittsburgh, PA, USA(e-mail address: kpekkan@andrew.cmu.edu)

This inter-disciplinary study conducted and supervised by joint senior authors Pekkan and Liu with equal contribution focusing bioengineering and clinical aspects respectively.

Keywords: Lateral Fontan, Intra-atrial conduit Fontan, Computational fluid dynamics, Fontan conversion, Fenestration

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ABSTRACT

Background: Intra-atrial conduit Fontan is regarded as a modification of both extra-cardiac and lateral tunnel Fontan. In this study, the patient-specific hemodynamic performance of intra-atrial conduit and lateral tunnel Fontan with conversion templates and fenestration is investigated based on our patient cohort. Methods: Computational fluid dynamics simulations are performed using patient-specific models of intra-atrial conduit Fontan and lateral tunnel Fontan patients. Real-time "simultaneous" inferior and superior vena cava, pulmonary artery and fenestration flow waveforms are acquired from ultrasound. Multiple hemodynamic performance indices were investigated for the evaluation of the pulsatile flow performance. Results: Power loss inside the lateral tunnel Fontan appeared significantly higher than the intra-atrial conduit Fontan for patient-specific cardiac output and normalized connection size. Inclusion of the 4 mm fenestration at 0.24L/min mean flow resulted in lower cavopulmonary pressure gradient and less time-averaged power loss for both Fontan connections. Flow-structures within the intra-atrial conduit were notability more uniform than the lateral tunnel. Hepatic flow favored majorly the left lung in both surgical connections: LT-to-IAC Fontan conversion resulted better hemodynamics with less power loss, pressure gradient, and stagnant flow zones along the conduit. Conclusions: Patient-specific computational case study demonstrated superior hemodynamics of intra-atrial conduit Fontan over lateral tunnel Fontan with or without fenestration and improved performance after the conversion of lateral tunnel to intra-atrial conduit. Geometry-specific effect of non-uniform hepatic flow distribution may motivate new rationales on the surgical design.

1. Introduction

Since its first description by Dr. Francis Fontan and Baudet in 1971, a variety of Fontan operation modifications have been developed for optimal hemodynamics and lesser complications. Among several surgical templates, two modifications that are used in common practice are lateral tunnel (LT) and extra-cardiac (EC) Fontan connections [6; 19]. In spite of their routine use, there is still a controversy on which type of Fontan template, EC or LT, provides superior outcome [2], as an "ideal" conduit suiting a particular patient. Intra-atrial conduit (IAC) Fontan is another connection template to facilitate Fontan completion with its intra-atrial conduit graft anastomosed to the internal orifice of the inferior vena cava (IVC). The conduit is then brought from the right atrial roof and is sutured with the pulmonary artery (PA). IAC is regarded as a modification of LT with a straighter, shorter conduit and potential to reduce arrhythmia due to lesser intra-cardiac surgical handling.

Advances in pre-surgical planning tools [7] provided a remarkable ability to quantify local hemodynamics [28] and enabled pre-surgical performance evaluation of complex congenital anatomies [30]. Prior pre-surgical planning studies investigated the comparative hemodynamics of more common surgical templates; EC vs. LT. Performance of IAC has received limited attention and was investigated based on idealized surgical templates at steady state flow conditions [13]. The present study focuses on the evaluation of IAC in comparison to an LT template incorporating patient-specific geometry and flow waveforms. Recently Dasi et al. has demonstrated the proper non-dimensional scaling of Fontan conduits [4], which incorporated the effects of cardiac output (CO), pulmonary flow split and conduit size (Power Loss divided by CO^3/BSA^2). This new power loss scaling index enables unbiased comparison of power loss between different patient-specific conduits at steady-flow conditions. Recent clinical studies [17] revealed the patient-to-patient variations of venous and pulmonary flow pulsatility (flow waveform phase difference, amplitude and frequency) and its influence of conduit power loss [9] , which is accounted by two additional clinical indices [8]. *Present study incorporates both of these recent developments with the patient-specific anatomical conduits and real-time flow waveforms first time in literature.* Another important novelty of the present study is the evaluation of time-dependent fenestration flows in patient-specific templates again first-time in literature. To our knowledge the hemodynamics of fenestration has been studied in only one preliminary *in silico* study by Pekkan et.al. [22], in *idealized* geometries at steady flow conditions.

2. Methodology

2.1 Patient-specific data set

Two Fontan patients, Table 1, with IAC and LT connections that are representative of the standard patient-specific surgical templates routinely practiced at Shanghai Children's Medical Center (SCMC) were administered in this study. Informed consent was obtained from the patients before study enrollment through the institutional review board of the Shanghai Jiaotong University Medical School. Cardiac magnetic

resonance imaging based 3D volume reconstructions were generated according to the previously reported protocols and software [23] (Figure 1).

Real-time flow waveforms at IVC, superior vena cava (SVC), right pulmonary artery (RPA) and fenestration are acquired through multi-channel simultaneous respiration and ECG synchronized Doppler echocardiography measurements (Figure 2) following previously published protocols [12, 11]. Recordings were performed 1 cm distal to the hepatic vein at IVC, 2 cm distal to the PA anastomosis at SVC, 3 cm distal to SVC at RPA, and at the locus of the right-to-left communication, i.e. fenestration hole (FEN), for six consecutive respiratory cycles. CO is verified based on a fixed cardiac index (3 L/min/m^2) [29] and BSA is 0.9 m^2 and 0.64 m^2 for the IAC and LT Fontan connections, respectively.

2.2 Computational fluid dynamics (CFD)

In this study, we simulated hemodynamics of 5 different conduit templates; IAC, LT, their fenestrated versions and LT to IAC conversion at *real-time* patient-specific pulsatile blood flow conditions. Mesh-independent CFD simulations employing hybrid unstructured grids are performed following the protocols reported earlier [21, 9] for the duration of the respiration cycle. Patient-specific flow waveforms synchronized with both respiration and ECG are imposed at the caval vessel inlets, RPA and fenestration outlets.

LT to IAC Fontan conversion procedure was performed *virtually in the computer* by replacing the atrial-patch with an intra-atrial conduit (18mm) through our *sketch-based* in-house surgical editing tool (Figure 1) [7]. Post-conversion acute LT cavopulmonary flow rate and waveforms are maintained to match the original LT patient-specific data. Additional computer models were generated to evaluate the effect of fenestration flow by closing the 4mm sized puncture hole virtually.

2.3 Performance parameters

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Multiple hemodynamic performance indices that govern the pulsatile hemodynamic performance of the surgical connections are investigated; cavopulmonary pressure gradient (CPPG), power loss, and hepatic flow distribution (HFD) to the PAs are calculated by time-averaging over the respiratory cycle. Additional indices to estimate the blood residence time in the conduit (RT), and to properly quantify the pulsatile behavior of Fontan venous flows [8] are reported.

As a surrogate measure of power loss the CPPG was calculated based on the difference between mean venae cavae pressure $(P_{IVC}+P_{SVC})/2$ and the bilateral PA pressure (P_{LPA}). Ensemble running-average of the power loss was reported through the numerical simulation of 10 converged respiratory cycles using the control volume approach [7]. Dense Lagrangian particle-tracking was employed to calculate HFD to the lungs [5]. .

Total caval flow pulsatility index (TCPI) represents the percentage of the fluctuating flow component of the total venous flow $Q_V(t)$ relative to the mean time-averaged total caval flow rate Q_{AVG}, Usually, caval flow waveforms appear periodic with a period; $T_{respiration}$ referring to the length of the respiration cycle.

$$TCPI(\%) = \frac{1}{T_{respiration}} \int_{0}^{T_{respiration}} \left| \frac{Q_v(t)}{Q_{AVG}} - 1 \right| dt \tag{1}$$

where, $Q_v(t) = Q_{IVC}(t) + Q_{SVC}(t)$.

RT has been commonly used to analyze the hemolytic and thrombosis risk of blood-wetted surfaces inside cardiovascular medical devices [15, 1]. Here, RT represents the blood washout time inside the surgical baffle and identifies the low velocity (stagnation) recirculation zones that increase thromboembolic risk - an important Fontan failure mode [3, 18]. To quantify the relative size and spatial location of the stagnation regions and to compare the surgical templates, a normalized RT threshold-based parameter; SFI (stagnant flow index), is introduced;

$$SFI(\%) = \frac{V_{stagnant}}{V_{total}} \times 100 \tag{2}$$

where V_{total} *and* $V_{stagnant}$ refers to the total volume of the conduit and the stagnant volumes respectively. Essentially, SFI quantifies the stagnant, i.e. high residence time, blood volume inside the conduit. In flow stagnation the blood particles reside longer than the time required for the mainstream flow to transverse the entire connection. Hence, flow particles with RT larger than the maximum RT (occurs at the outlet boundaries) will not leave the flow domain and generate $V_{stagnant}$. Previously, Itatani et al. investigated the flow stagnation volume based on an arbitrary low velocity threshold (less than 0.01 m/s) to identify the optimal conduit size for EC Fontan operation [14]. Similar to RT, the low velocity threshold within the stagnation zone depends on the patient-specific conduit size and CO. Therefore, SFI incorporates the RT of the slowest particle leaving the flow domain as a threshold and provides a *normalized method (for unbiased patient-to-patient comparison)* to identify the size of the regions with low velocity or recirculation.

3. Results

3.1 Flow structures

As illustrated in Figure 3, the time-averaged 3D flow structures were significantly different for the surgical templates studied. LT model is dominated by IVC jet flow impinging on the posterior atrial wall, associated with the narrow inlet area of the IVC anastomosis with peak flow velocity range 0.5-1.5 m/s at the IVC orifice before diffusing laterally. Anterograde IVC flow exist solely on the left anterior-posterior wall of the connection, whereas, the right lateral side of connection was dominated by retrograde flow and generated a strong mixing pattern within the connection throughout the respiration cycle. In contrast, the IAC exhibited a uniform flow profile within IVC conduit. Due to the curvature variation, flow skewed slightly towards posterior wall by the IVC-to-conduit anastomosis and then towards anterior wall at the conduit-to-pulmonary artery anastomosis. RT iso-contours, Figure 4, highlighted a large stagnation zone, which initiates at the orifice of the IVC anastomosis and resides along the anterior wall of LT anatomy. Due to the pulsatile oscillations on the IVC flow, boundaries of the stagnation zone moved within the surgical connection and resulted bidirectional flow patterns at the bulging section. For the IAC geometry, proximal to the conduit-to-pulmonary artery anastomosis, flow separated severely from the connection and formed a stagnant zone on the

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posterior wall. Still, the regions with high RT were significantly smaller, stable and confined proximal to the boundary layer of the IAC throughout the respiration cycle.

3.2 Comparison of patient-specific LT Fontan and IAC Fontan performance

Hemodynamic performance of the patient-specific Fontan templates with different cavopulmonary pulsatility scenarios is summarized in Table 2. For the patient-specific settings, time-averaged power loss for the LT connection was significantly higher (almost two folds) than IAC Fontan geometry. Likewise, CPPG across the LT connection and SFI were calculated higher in comparison to IAC Fontan geometry (1.7 versus 0.8 mm Hg, respectively). For both surgical connections, HFD was very non-uniform and favored majorly the left lung. Still, HFD to left versus right lung appeared relatively more uniform for the LT (83:17) in comparison to the IA connection (94:06). Quantification of the caval flow pulsatility indicated higher mean pulsatile content (56%) for LT waveforms, which contributed to higher conduit power losses [9].

For an unbiased comparison between patient-specific surgical templates, it is essential to delineate the factors that affect hemodynamic loading within a cavopulmonary connection [4] . In this study, we also performed a performance comparison for IAC and CO/SIZE matched LT Fontan patients (Table 2). After CO/SIZE matching, time-averaged power loss, and CPPG were even higher than these parameters without CO/SIZE matching. Neither HFD nor SFI changed significantly after CO/SIZE matching.

3.3 Hemodynamic performance after Fontan conversion

LT to IAC Fontan conversion decreased the axial flow velocity within the tunnel/conduit-pulmonary anastomosis and the reduced the stagnant zone along the conduit as shown in Figure 4. SFI decreased significantly after conversion (38 versus 29). Particularly regions with high RT along the original atrial-patch were reduced by 30%– a major improvement. The conduit power loss and CPPG were reduced by 10% and

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0.5 mm Hg, respectively, after the conversion. Fontan conversion caused notably less uniform HFD to the left and right lungs, i.e. 95:5 for post-conversion versus 87:13 for pre-conversion.

3.4 Hemodynamic evaluation of fenestration

4 mm fenestration hole exhibited geometry-specific effects on the time-averaged conduit flow structures and hemodynamic performance. With fenestration, more IVC flow was redistributed circumferentially within the surgical connection and axial flow speed was decreased. Flow stagnation inside the LT geometry, particularly at the posterolateral atrial-patch wall and proximal to IVC-to-pulmonary-artery anastomosis was increased (8%). Removal of the fenestration flow (~10% CO) yielded 10% increase in power losses inside the LT Fontan geometry, whereas no notable change in IAC Fontan geometry. For both models the time-averaged CPPG was elevated slightly after fenestration closure.

Removal of the fenestration yielded 19% elevation in hepatic flow to RPA for the LT connection, though 6% increase for the IAC. Despite the reduction of net hepatic flow reaching the lungs (up to 40%) due to the right-to-left shunt, fenestration showed almost no effect on the percent HFD to the lungs. Relatively higher influence of the fenestration closure on IAC conduit performance was, in part, due to the larger average fenestration flow rate (0.37 L/min) in comparison to LT model (0.27 L/min).

4. Discussion

Power losses and hemodynamic performance of a cavopulmonary connection depends on: (i) cardiac output (BSA, cardiac index) [4], (ii) 3D geometric features (conduit versus atrial patch), (iii) size i.e. area/volume of the surgical connection (BSA, age), (iv) time-dependant flow splits at the pulmonary arteries and (v) pulsatility of cavopulmonary flow waveforms [9]. In this study, we performed both patient-specific and unbiased (CO and size matching) pulsatile hemodynamics comparison between IAC and LT Fontan. Incorporating an expanded set of performance parameters, IAC Fontan has superior hemodynamics than LT Fontan. Detailed flow analysis indicated that decreased hemodynamic performance of the LT model was

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primarily due to the sudden expansion of IVC flow into the dilated atria, which formed a highly dissipative free-shear layer on the posterior wall, generated secondary flow vortices and a large stagnant flow zone inside the connection.

Thromboembolic complications with an incidence of 9% to 33% have been reported as the significant contributor to morbidity and mortality after the Fontan operation [26]. Possible flow stasis through the Fontan pathway is regarded as one of main factors for these events. Analysis throughout the respiration cycle is found to be critical for accurate thromboembolic assessment. Flow in LT Fontan is unevenly distributed within the connection; a large stagnant flow zone is initiated by the orifice of the IVC anastomosis, which spanned from the IVC to the anterior wall of the Gortex patch. In contrast, flow within the IAC is significantly more uniform and has less stagnant regions than LT.

For the patients in developing countries, where the timing of the first stage operation may not always be optimal, fenestration is likely to reduce morbidity and mortality. Inclusion of fenestration is a routine procedure in our center for the majority of IAC and LT Fontan patients, but not for EC, as it can exuberate additional technical challenges [24]. The results shows that fenestration decrease CPPG inside the cavopulmonary anatomy in both IAC and LT Fontan, which agree with the former reports that fenestration decrease early postoperative pleural effusion and shorten hospital stay by decompression of prepulmonary venous pressure [20, 12, 10]. Another interesting finding of fenestration hemodynamics is that it leads to an increase in SFI in LT but not in IAC connection. Despite the apparent benefits of fenestration, one of major drawbacks is the risk of systemic embolization due to the paradoxical shunt direction close to fenestration area [10; 25]. More uniform flow and potentially lower embolization risk of IAC indicate its superior surgical design over LT.

Liver-driven hepatic factors are required for preventing arterio-venous malformations (PAVMs) and to ensure normal development of lungs. For both templates the right lung received significantly less IVC flow in comparison to the left lung. RPA to IVC flow ratio (RPA/IVC) was 3% and 13% for IAC and LT geometries,
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respectively, primarily due to high SVC flow. In agreement with Ref. [27, 16], we believe that the reason is that the mean SVC flow dominates the IVC flow in young age population and the surgical offset between SVC to IVC has mechanical impetus for routing IVC flow to the lung of the same side. This highlights the importance of connection geometry on the TCPC connection by modulating the pathway of the IVC flow jet and mixing with SVC, especially in the patients with high risk of PAVMs like left isomerism with azygous continuation of the IVC.

To improve the performance of the LT connection, we evaluated the hemodynamic performance of LT-to-IAC Fontan conversion by virtually replacing the atrial patch with a 18 mm size conduit. Our results showed significant reductions on the flow stagnation zone and improvements on the conduit energy efficiency after the conversion. As the size mismatch between relatively smaller cavopulmonary anatomy and the 18 mm conduit decreases during the somatic growth, we expect the hemodynamic performance of the new connection to increase further. In our institute, Fontan conversions have been performed to *rescue* failed Fontan circulations, patients with dilated right atrium, large thrombus in right atrium and atrial tachyarrhythmias. Therefore, these results provide the technical insight for surgeons on the utility of IAC as another alternative for Fontan conversion.

5. Limitations

This study is clearly limited by the small study size although this concern may be tempered by the unbiased (CO and size matching) hemodynamics comparison in method and the visual LT-to-IA conversion as well. A larger series of Fontan patients' MRI data incorporating clinical data is necessary to apply the finding to the whole LT and IAC Fontan population in the future.

6. Conclusion

For the selected patient-specific cavopulmonary anatomies and venous flows, hemodynamic performance of the IAC Fontan connection was superior to the LT Fontan geometry with or without fenestration based on lower power losses and pressure gradient, and better local hemodynamics (less stagnant flow zones). Early post-op evaluation of LT-to-IAC conversion facilitates improved hemodynamics by reducing both power loss and flow stagnation zones significantly. Longitudinally, the benefit of the conversion may be more pronounced as the patient-baffle size mismatch decreases by early adulthood. Geometry-specific effect on non-uniform HFD may motivate new rationales on the surgical design.

Acknowledgments

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Table 1: Representative patients selected and basic demographics information.

Table 2: Summary of hemodynamic performance evaluation based on the conduit power losses (PL), cardiopulmonary pressure gradient (CPPG), hepatic flow distribution (HFD), high residence time volume ratio (SFI) and total caval flow pulsatility index (TCPI) for the patient-specific intra-atrial conduit (IAC), lateral tunnel Fontan (LT) and LT to IAC conversion connections with and without fenestration.

Table1

	Age (y)	Weight (kg)	BSA (m^2)	Diagnosis	Procedure
Patient 1	6	22	0.90	DORV, Supero-inferior ventricles, PS	IAC
Patient 2	3	16	0.64	TGA, PS	LT

Table 2

Model	Power Loss (mW)		CCPG (mm Hg)		HFD (LPA/RPA)		SFI (%)		TCPI (%)
	fen	*no-fen*	*fen*	*no-fen*	*fen*	*no-fen*	*fen*	*no-fen*	
IAC	1.55	1.59	0.8	1.0	94:06	94:06	15	15	16
LT	2.74	3.01	1.7	1.9	83:17	83:17	38	33	25
LT (CO/SIZE matched)	3.77	-	2.1	-	83:17	-	36	-	25
LT to IAC	2.34	-	1	-	95:05	-	29	-	25

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Figure 1: Three-dimensional volumetric reconstructions. Inta-atrial conduit (IAC) Fontan with fenestration, lateral tunnel (LT) with fenestration, and conversion from LT-IAC tunnel models. Arrow indicates the location of fenestration hole.

Figure 2: Time-resolved Doppler ultrasound flow waveforms of lateral tunnel (TOP) and intra-atrial conduit (BOTTOM) Fontan patients, synchronized with respiration and ECG signals, shown for one respiration cycle. Flow waveforms at inferior vena cava (IVC), superior vena cava (SVC) are imposed as the inlet flow boundary condition, whereas, right pulmonary artery (RPA) and fenestration (FEN) flow waveforms are assigned at the outlets of the computational models.

Figure 3: Contour maps colored with velocity magnitude for intra-atrial conduit (IAC) and lateral tunnel (LT) Fontan connections, post-op Fontan conversion and, IAC and LT connections after fenestration closure, shown in anterior (TOP ROW) and posterior (BOTTOM ROW) views at multiple orthogonal planes illustrating the major flow structures within the conduit.

Figure 4: Time-averaged streamlines and iso-contours within the intra-atrial conduit (a), lateral tunnel (b) Fontan connections and Fontan conversion (c) colored with flow velocity and fluid residence time (RT). RT iso-contours are shown for $RT > RT_{outlet}$, i.e. maximum RT at the outlet boundaries in order to display the stagnation zones that resides inside the connections. Fenestration holes (4.0 mm diameter) are marked with red arrows.