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The influence of systemic-to-pulmonary arterial shunts and peripheral vasculatures in univentricular circulations: Focus on coronary perfusion and aortic arch hemodynamics through computational multi-domain modeling

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ABSTRACT

Initial palliation for univentricular hearts can be achieved via a systemic-to-pulmonary shunt (SPS). SPS configurations differ depending on the proximal anastomosis location, which might lead to dissimilar coronary and upper body perfusions. Mathematical modeling can be used to explore the local and global hemodynamic effects of the SPSs. In literature there are few patient-specific models of SPS that specifically address the influence of both the local and peripheral vasculature. In this study, multi-domain models of univentricular circulations were developed to investigate local hemodynamics and flow distribution in the presence of two shunt configurations. We also analyzed the relative impact of local and peripheral vascular resistances on coronary perfusion and flows through the upper aortic branches.

A two-step approach was followed. First, two patient-specific models were based on clinical data collected from univentricular patients having different shunts and peripheral vasculatures. Each model coupled a three-dimensional representation of SPS, aortic arch (AA) and pulmonary arteries, with a lumped parameter model (LPM) of peripheral vasculature closing the circulatory loop. Then, two additional models of hypothetical subjects were created by coupling each customized LPM with the other patient's three-dimensional anatomy.

Flow rates and pressures predicted by the patient-specific models revealed overall agreement with clinical data. Differences in the local hemodynamics were seen during diastole between the two models. Varying the three-dimensional models, while keeping an identical LPM, led to comparable flow distribution through the AA, suggesting that peripheral vasculatures have a dominant effect on local hemodynamics with respect to the shunt configuration.

1. Introduction

In clinical practice, cyanotic congenital heart diseases in the setting of univentricular hearts can be initially palliated with a systemic-to-pulmonary shunt (SPS). This is typically constructed by placing a synthetic conduit between the systemic and pulmonary arterial circulations, which increases pulmonary blood flow and relieves cyanosis. In this circulation, the systemic and pulmonary arterial blood flows are in parallel, driven by the single ventricular pump. However, the optimal balance between systemic and pulmonary perfusion can be a challenge to achieve since SPS directly impacts on how much blood in entering the pulmonary and systemic circulations. Thus, a well-functioning SPS should achieve adequate systemic oxygenation and systemic/coronary perfusion to allow the patient to grow and thrive to further along the single ventricle palliation pathway.

Currently, there are multiple manners in which SPS can be constructed, depending on where the shunt takes off the systemic arterial tree. The most frequent SPS is the modified Blalock-Taussig shunt (MBTS), which typically originates from the innom-

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Nomenclature

AA	aortic arch
CS	central shunt
DA	descending aorta
IA	innominate artery
LB	lower body
LCA/RCA	left/right carotid artery
LPM	lumped parameter model
LSA/RSA	left/right subclavian artery
MBTS	modified Blalock-Taussig shunt
MRI	magnetic resonance imaging
PVR	pulmonary vascular resistance
SPS	systemic-to-pulmonary shunt
$SVR_{UB/LB}$	upper/lower body systemic vascular resistance
UB	upper body
3D	three-dimensional

inate artery (IA). A central shunt (CS) connects the ascending aorta to the pulmonary artery, while the right ventricle-pulmonary artery shunt derives from the right ventricle (Gaca et al., 2008). An alternative central connection could be made through the Melbourne shunt i.e., a direct aorto-pulmonary anastomosis (Mumtaz et al., 2008). In addition to being subjected to high pressure gradients and varying flow pulsatility due to the restrictive nature of the shunt between the high-pressured systemic and low-pressured pulmonary circulations, a SPS often develops uneven intraluminal narrowing (due to intimal hyperplasia) or curvature distortion during the first months after implantation (Bonnet et al., 2015; Celestin et al., 2015). Blood flow within the coronary, systemic and pulmonary (via the SPS) circulations depends on local anatomy and downstream resistances. Hence, different locations of the anastomotic site as well as different peripheral vasculatures might lead to dissimilar coronary and upper body (UB) perfusions.

Mathematical modeling is a tool widely used to explore complex fluid dynamics such as those characterizing SPSs and the neighboring native vessels (Biglino et al., 2013). It allows to compute hemodynamic variables for different shunt configurations and varying anastomosis angles (Ding et al., 2013; Hsia et al., 2011; Laganà et al., 2005; Migliavacca et al., 2000; Mroczek et al., 2011; Piskin et al., 2017; Qian et al., 2010; Zhao et al., 2015), and to improve the understanding of pathophysiological processes occurring in such circulatory settings (Celestin et al., 2015; Waniewski et al., 2005). Most of the literature models are either realistic (Hsia et al., 2011; Moghadam et al., 2012) or simplified (Di Molfetta et al., 2016; Ding et al., 2013; Shimizu et al., 2016; Zhao et al., 2015). Nevertheless, for an accurate and consistent reproduction of the aortic arch (AA) hemodynamics of first-stage patients, patient-specific models are required. Some groups reconstructed customized three-dimensional (3D) models of the AA and PAs but they imposed realistic boundary conditions in an open-loop fashion (Piskin et al., 2017; Wang et al., 2015). Since both local anatomy and peripheral resistances are crucial for AA flow distribution, closed-loop multi-domain models allow one to account for the two elements interdependence. Only in two recent works both the 3D geometry and the lumped parameter model (LPM) closing the circulatory loop were customized (Arthurs et al., 2017; Zhao et al., 2015). However, the studies reproduced several SPS configurations as virtual surgeries, by either disregarding possible changes in the shunt lumen during the months preceding second-stage palliation (Zhao et al., 2015), or applying unrealistic constant lumen reduction (Arthurs et al., 2017). Since univentricular patients typically undergo a second-stage palliation at 4–6 months of life, clinical data are usually obtained immediately before surgery. At that time, it is likely that shunt geometry appears different from the implanted look i.e., with variable and distorted diameter along the axis.

The present study has two main goals: (1) to develop accurate patient-specific models of first-stage circulations allowing for local fluid dynamics and flow distribution analysis in the presence of two different shunt configurations (MBTS vs. CS); (2) to investigate the relative influence of local (i.e., shunt configuration and AA shape) and peripheral vascular resistances on coronary perfusion and flows through the upper aortic branches.

2. Materials and methods

This study utilized clinical data acquired from two univentricular patients, A and B, that were recruited to the Medical University of South Carolina, Charleston, SC, and the University of Michigan, Ann Arbor, MI, respectively. The local institutional review boards approved the study.

2.1. Patient-specific multi-domain models

In order to develop multi-domain patient-specific models, first we created preliminary stand-alone LPMs of the patients' circulations using Matlab (MathWorks, Inc., MA, USA). To this end, we adopted a methodology similar to that described by Corsini et al. (2014). Based on flow and pressure data (Table 1) that were acquired from patients A and B at the time of second-stage surgery, pulmonary vascular resistance (PVR) and systemic vascular resistances of the upper body (SVR_{UB}) and lower body (SVR_{LB}) were estimated for each patient (Table 1). Global resistance values were used to derive individual resistances, compliances and inertances of the systemic and pulmonary blocks with the scaling approach presented by Corsini et al. (2014). The LPM layout (Fig. 1) was analogous to that developed in that study as for the univentricular heart, UB and SPS. By contrast, not being the focus of this study, the lower body (LB) and pulmonary circulation models were fur-

Table 1
Clinical data acquired from the two patients and estimated vascular resistances.

	Patient A (MBTS)	Patient B (CS)
HR (bpm)	107–109[a]; 113–129[b]	115–132[a]; 108–118[b]
CO (ml/s)	20.4	24.4
Q_P (ml/s)	9.7	7.5
Q_{UB} (ml/s)	5.2	11.2
Q_{LB} (ml/s)	5.5	5.7
P_{AT} (mmHg)	6	5
P_{PA} (mmHg)	12	13
P_{AO} (mmHg)	52	43
$P_{V\text{-}max}$ (mmHg)	95	103
PVR (WU m^2)	3.08	6.04
SVR_{UB} (WU m^2)	44.1	19.2
SVR_{LB} (WU m^2)	42.4	37.8

HR: heart rate; bpm: beats/min; CO: cardiac output; Q_P: pulmonary flow; Q_{UB}: upper body flow; Q_{LB}: lower body flow; P_{AT}: atrial pressure; P_{PA}: pulmonary artery pressure; P_{AO}: aortic pressure; $P_{V\text{-}max}$: maximum ventricular pressure. See the nomenclature for the acronyms of resistances. PVR, SVR_{UB} and SVR_{LB} were calculated as the ratios between pressure drops and flow rates: $PVR = (P_{PA} - P_{AT})/Q_P$; $SVR_{UB} = (P_{AO} - P_{AT})/Q_{UB}$; $SVR_{LB} = (P_{AO} - P_{AT})/Q_{LB}$. 1 WU (Wood Units) = 1 mmHg min/L.
[a] Range measured during MRI.
[b] Range measured during cardiac catheterization.

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