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Superior performance of continuous over pulsatile flow ventricular assist devices in the single ventricle circulation: A computational study

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ABSTRACT

This study compares the physiological responses of systemic-to-pulmonary shunted single ventricle patients to pulsatile and continuous flow ventricular assist devices (VADs). Performance differences between pulsatile and continuous flow VADs have been clinically observed, but the underlying mechanism remains poorly understood. Six systemic-to-pulmonary shunted single ventricle patients (mean BSA=0.30 m^2) were computationally simulated using a lumped-parameter network tuned to match patient specific clinical data. A first set of simulations compared current clinical implementation of VADs in single ventricle patients. A second set modified pulsatile flow VAD settings with the goal to optimize cardiac output (CO). For all patients, the best-case continuous flow VAD CO was at least 0.99 L/min greater than the optimized pulsatile flow VAD CO ($p=0.001$). The 25 and 50 mL pulsatile flow VADs exhibited incomplete filling at higher heart rates that reduced CO as much as 9.7% and 37.3% below expectations respectively. Optimization of pulsatile flow VAD settings did not achieve statistically significant ($p<0.05$) improvement to CO. Results corroborate clinical experience that continuous flow VADs produce higher CO and superior ventricular unloading in single ventricle patients. Impaired filling leads to performance degradation of pulsatile flow VADs in the single ventricle circulation.

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1. Introduction

Children born with single ventricle congenital heart defects require staged surgical intervention to enable survival. The first of three stages involves insertion of a systemic-to-pulmonary shunt that provides the infant's only source of pulmonary blood flow. However, patients remain at risk of heart failure (HF) due to increased volume loading on the single working ventricle (Gewillig, 2005). A ventricular assist device (VAD) can be used as mechanical bridge support for these patients. VADs have been used in single ventricle circulations (Calvaruso et al., 2007; Cardarelli et al., 2009; Chu et al., 2007) and normal circulations (Adachi and Fraser, 2011; Hetzer et al., 2006b; Stiller et al., 2003), but survival rates for pediatric patients with congenital heart defects remain approximately 25% lower than those without (Morales et al., 2010) and outcomes worsen further in single ventricle cases. Therefore, increased knowledge of mechanisms affecting VAD performance in single ventricle circulations is needed to improve clinical outcomes for these patients.

VADs can be categorized as either pulsatile or continuous flow. Pulsatile flow VADs emulate the heart's distinct phases of diastole and systole. The Berlin Heart EXCOR VAD remains the only such FDA approved device for infants. VAD blood flow is driven via

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membrane, and valves are located at the inlet and outlet of this "ventricle." Membrane motion is controlled by an air chamber connected to an external air compressor. By contrast, continuous flow VADs use rotors to produce a pressure rise for a particular flow and rotational speed (Moazami et al., 2013). Continuous flow designs generally have better reliability and smaller size while reducing risk of infection, bleeding, trauma, and thrombus (Cheng et al., 2014; Drews et al., 2008; Feller et al., 2007; Kato et al., 2011). While continuous flow devices are now used extensively in adults and older children, none are specifically designed for long-term use in infants. Successful bridge treatment of pediatric patients with continuous flow VADs has been demonstrated (Miera et al., 2011), however further experience is needed in single ventricle circulations. Studies have suggested pulsatile flow VADs may promote better ventricular unloading and more natural physiology (Cheng et al., 2014; Drews et al., 2008; Klotz et al., 2004), however continuous flow VADs may encourage faster recovery of myocardial tissue due to less pulsatile trauma on the heart tissue (Frazier et al., 2004; Frazier and Myers, 1999).

Computational simulations of the cardiovascular system can model the interaction of VADs and other devices with circulatory physiology and predict hemodynamics. Lumped-parameter networks (LPN) and state space models offer a reduced-order modeling approach by making an analogy to electrical circuits and forming a system of ordinary differential equations (ODEs) solved by numerical integration (Ferreira et al., 2005; Kung et al., 2014). In this study, we will use an LPN model to assess VAD performance for our patient cohort. Three dimensional computational fluid dynamics (CFD) methods can obtain greater hemodynamic detail (Migliavacca et al., 2006; Peng et al., 2012), but coupling of VAD CFD simulations to physiologic models has only recently been accomplished (Neidlin et al., 2016). This study improves over the previous work by incorporating a model describing ventricular suction induced by a VAD.

This study aims to understand physiological responses of stage 1 single ventricle patients to pulsatile and continuous flow VADs and to identify mechanistic explanations for differences in performance. This will be evaluated on cohort and patient specific levels. Recommendations for achieving optimal VAD performance in single ventricle patients will be provided within operational limitations of the VADs.

2. Methods

2.1. Overview of study

The LPN used in this study (Fig. 1) was based on our previous work (Kung et al., 2014). To simulate VAD support, the inflow and outflow cannulas were connected to the ventricle and aorta respectively. In clinical practice, the outflow cannula could be attached to one of several locations near the aorta, such as the neoaorta or innominate artery. In the LPN, which is a simplified representation of vasculature, these locations each correspond to the aortic node. A connection between the aorta and pulmonary arteries represented the systemic-to-pulmonary shunt. Respiration effects were assumed negligible.

Clinical measurements from six stage 1 single ventricle patients (cohort body surface area (BSA) range 0.26–0.34 m^2; mean 0.30 m^2) were obtained from the Great Ormond Street Hospital, Medical University of South Carolina, and University of Michigan. For the LPN simulations to accurately replicate each patient's unique physiology, the LPN element values were tuned using a process similar to our previous works (Corsini et al., 2015, 2014; Kung et al., 2013) to match individual patient's clinical measurements. Once tuning was complete, ventricular contractility was set to zero to simulate HF.

2.2. Simulation setup and protocol

We have previously reported a clinical case of extracorporeal implementation of the Revolution VAD (Sorin Group, Italy) in a stage 1 single ventricle patient via 9 mm inner diameter (ID) Berlin Heart cannulas (Lal et al., 2014). However, insufficient data existed to construct a computational model for the Revolution VAD. Therefore, we constructed a HeartWare VAD (HeartWare Inc., Framingham, Massachusetts) model for this study to resemble the continuous flow VAD scenarios similar to our previous clinical experience. Due to the similar continuous flow centrifugal designs of the HeartWare and Revolution VADs, they would produce the same hemodynamics when generating the same pressure head. The only variable setting for the continuous flow VAD was revolutions per minute (RPM).

We modeled the Berlin Heart EXCOR VAD (Berlin Heart GmbH, Berlin, Germany) for the pulsatile flow scenarios in this study. Variable VAD settings for the Berlin Heart were the device size, "heart rate" (HR), peak filling (P_{DIA}) and ejection (P_{SYS}) pressures, and diastolic filling ratio (DFR), which is the time ratio of diastole to the total VAD period.

Two primary sets of simulations were done. The first emulated current clinical implementation of VADs specific to stage 1 single ventricle patients. The pulsatile flow VAD was simulated with the following ranges of settings: HR (15–105 BPM for 10 and 25 mL, 15–75 BPM for 50 mL), P_{DIA} (−40 mmHg), P_{SYS} (mean aortic pressure+100 mmHg), and DFR (60%). The continuous flow VAD was simulated with rotor speeds from 1800–3400 RPM. Cannula dimensions (Table 1) specified by the manufacturers were used. The second set of simulations investigated changes to pulsatile flow peak pressure and DFR settings to optimize cardiac output.

The system of ODEs describing the LPN were solved with a fourth order Runge-Kutta time-integration method using FORTRAN (IBM Corp., Armonk, New York), and data were analyzed using MATLAB (MathWorks Inc., Natick, Massachusetts). After simulations reached periodicity, data from the last cardiac period were used in the analyses.

2.3. Statistics

To determine statistical significance, hypothesis testing with p-values was done assuming a normal distribution. For this study, the null hypothesis was that there is no difference in results between two samples. The threshold for statistical significance was 0.05. The t-statistic was used, and the probability for a two-tailed distribution was calculated.

2.4. Ventricular assist device modeling

2.4.1. Pulsatile flow VAD

The Berlin Heart comes in several sizes ranging from 10 to 80 mL. The 10 and 25 mL sizes are common for pediatric use (Hetzer et al., 2006a; Stiller et al., 2003), and the 50 mL size is also occasionally used to achieve higher CO. Since the Berlin Heart is controlled by the external air compressor, the model prescribed VAD pressure, P_{COMP}, as a sinusoidal function (Fig. A1)

$$P_{COMP} = \begin{cases} P_{SYS}\left(\sin\left(\frac{t*\pi}{(1-DFR)*t_{VAD}}\right)\right)^{0.1} & systole \\ P_{DIA}\ \sin\left(\frac{(t-(1-DFR)*t_{VAD})*\pi}{DFR*t_{VAD}}\right) & diastole \end{cases} \quad (1)$$

where t_{VAD} is the time of one VAD period and DFR is the diastolic filling ratio (a number between zero and one). The air compressor is limited to HRs up to approximately 110, 100, and 60 BPM for the 10, 25, and 50 mL sizes respectively.

2.4.2. Continuous flow VAD

For continuous flow VADs, little pulsatility exists once equilibrium occurs between the VAD and the patient's physiology. We used experimental data from literature for the HeartWare VAD to create trendlines (Fig. A2) in the form

$$\Delta P_{VAD} = AQ_{VAD}^2 + BQ_{VAD} + C \quad (2)$$

where ΔP_{VAD} is the pressure rise across the VAD, Q_{VAD} is the flowrate through the VAD, and A, B, and C are constants dependent on the VAD RPM (Moazami et al., 2013).

2.5. Ventricular suction caused by VAD operation

We define resistance due to ventricular collapse induced by a VAD as the ventricular suction resistance, R_{SUC} (mmHg.s/mL). If the VAD attempts to draw blood from the ventricle below its reference volume, which results in a negative ventricular pressure, the ventricle begins to collapse. When this occurs, tissue may be drawn into the cannula or the septum may be drawn closer to the cannula (Salamonsen et al., 2015), both of which can inhibit blood flow. Several models have been proposed in literature (Choi, 1998; Lim et al., 2010; Schima et al., 1990; Yu and Porter, 2006) to describe ventricular suction resistance induced by VADs in various animal experiments.

The ventricular suction models from these previous studies did not produce suction responses during continuous flow VAD simulations consistent with our clinical observations. Therefore, we developed a new model containing two components that improve its realism (Appendix B). We first developed an allometric scaling law relating R_{SUC} to BSA to generalize the model. Second, we combined experimental data from several prior works to create a ventricular suction model

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