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Continuous and Pulsatile Pediatric Ventricular Assist Device Hemodynamics with a Viscoelastic Blood Model

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Abstract

Purpose—To investigate the effects of pulsatile and continuous pediatric ventricular assist (PVAD) flow and pediatric blood viscoelasticity on hemodynamics in a pediatric aortic graft model.

Methods—Hemodynamic parameters of pulsatility, along with velocity and wall shear stress (WSS), are analyzed and compared between Newtonian and viscoelastic blood models at a range of physiological pediatric hematocrits using computational fluid dynamics.

Results—Both pulsatile and continuous PVAD flow lead to a decrease in pulsatility (surplus hemodynamic energy (SHE), ergs/cm³) compared to healthy aortic flow but with continuous PVAD pulsatility up to 2.4 times lower than pulsatile PVAD pulsatility at each aortic outlet. Significant differences are also seen between the two flow modes in velocity and WSS. The higher velocity jet during systole with pulsatile flow leads to higher WSSs at the anastomotic toe and at the aortic branch bifurcations. The lower velocity but continuous flow jet leads to a much different flow field and higher WSSs into diastole. Under a range of physiological pediatric hematocrit (20-60%), both velocity and WSS can vary significantly with the higher hematocrit blood model generally leading to higher peak WSSs but also lower WSSs in regions of flow separation.

Conclusions—The large decrease in pulsatility seen from continuous PVAD flow could lead to complications in pediatric vascular development while the high WSSs during peak systole from pulsatile PVAD flow could lead to blood damage. Both flow modes lead to similar regions prone to intimal hyperplasia (IH) resulting from low time-averaged WSS (TAWSS) and high oscillatory shear index (OSI).

Keywords

pediatric; PVAD; viscoelastic; hematocrit; hemodynamics; end-to-side anastomosis; CFD

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Introduction

Congenital heart disease affects over 1.35 million newborns annually worldwide [1] with heart transplantation the only option for many. Additionally, infants waiting a heart transplantation face the highest wait-list mortality among all of transplantation medicine with 23% dying within 6 months of being added [2]. Despite this, only recently has a pediatric ventricular assist device (PVAD), the Berlin Heart EXCOR, been approved for use in the United States as a bridge to transplantation for children of various sizes [3]. To help improve the outcomes for these patients, the National Institutes of Health (NIH) started the National Heart, Lung and Blood Institute (NHLBI) Pediatric Circulatory Support Program in 2004 and awarded five contracts with the goal of creating mechanical circulatory support devices for children ranging from 2-25 kg [4]. Three of those contracts were for the development of continuous blood flow devices, one was the Penn State PVAD pulsatile device based on the adult pneumatic Pierce-Donachy/Thoratec device and the last was a pediatric cardiopulmonary assist system that can deliver both continuous and pulsatile flow.

Over the past few decades, clinical investigations and animal experiments have shown that pulsatile perfusion during CPB is more beneficial to patients than nonpulsatile flow [5]. Pulsatile flow is able to significantly improve blood flow to vital organs including the brain and kidneys [6], heart [7], liver [8], pancreas [9], and the gastrointestinal system [10]. More hemodynamic energy is generated during pulsatile flow compared to nonpulsatile flow resulting in improved microcirculation and metabolism in patients on CPB [11-13]. Additionally, in contrast to early studies of extracorporeal circulation where hemolysis and platelet destruction were cited as disadvantages of pulsatile flow [14,15], more recent studies have shown that pulsatile cardiopulmonary bypass (CPB) flow is no more damaging to red blood cells and platelets than nonpulsatile flow [16,17].

Left ventricular aortic bypass is widely used for the implementation of both adult VADs and PVADs. The VAD outflow graft is attached via an end-to-side anastomosis to the ascending aorta of the patient. Intimal hyperplasia (IH), due to smooth muscle proliferation and matrix deposition, is a cause of long-term failure of end-to-side anastomotic grafts [18, 19]. Ku *et al.* [20], in a carotid bifurcation, found strong correlations between intimal thickening (IT) and several wall shear stress (WSS) effects including the inverse of maximum WSS, inverse of mean WSS, and oscillatory shear index (OSI), a ratio of time duration of retrograde to antegrade WSS. Common locations of IT in an anastomosis are the heel, toe and graft floor of the anastomosis. The toe and heel are regions of flow separation and high spatial gradients of WSS while the graft floor experiences low WSS due to a stagnation point flow created as flow divides between the proximal and distal outflow segments [21].

Previous computational fluid dynamics (CFD) studies have been performed on both adult and pediatric aortic geometries to try and understand their complex hemodynamics. Analysis of both continuous [22, 23] and pulsatile [24] aortic graft flow in adult ascending aorta geometries have been performed. Resultant hemodynamics in pediatric Fontan flow [25] and in pediatric aortic graft flow under both continuous and pulsatile conditions [26, 27] have also been studied. All of these previous studies have modeled blood as a Newtonian fluid. It is known, however, that blood is a viscoelastic fluid with a non-uniform viscosity and

elasticity that vary with shear rate. Additionally, neonate and pediatric blood, compared to adult blood, has a much lower plasma viscosity and decreased red blood cell (RBC) aggregation at low shear rates due to decreased plasma protein concentration [28] and a wide variability in patient hematocrit [29-31]. Several numerical and CFD studies have examined blood flow using general non-Newtonian models: Johnston *et al.* looked at the influence of non-Newtonian properties on both steady and transient blood flow in coronary arteries [32, 33], Chen *et al.* [34] and O'Callaghan *et al.* [35] investigated the non-Newtonian effects on hemodynamics in vascular grafts. Far fewer studies have examined the full viscoelastic nature of blood: Leuprecht and Perktold [36] studied the influence of viscoelastic effects of blood flow in a stenosed blood vessel and a 90° curved tube, Bodnar *et al.* [37] studied the viscoelastic effects of blood numerically in a stenosed vessel and carotid bifurcation and Good *et al.* [38] used a viscoelastic blood model to study pediatric blood flow in a healthy aorta. However, no viscoelastic blood models have been used to investigate pediatric graft flow or to compare continuous and pulsatile PVAD hemodynamics.

The purpose of this study is to investigate the effects of pulsatile and continuous PVAD flow mode and pediatric blood viscoelasticity on hemodynamics in a pediatric aortic graft model. Hemodynamic parameters of pulsatility, along with velocity and WSS, are analyzed and compared between Newtonian and viscoelastic blood models at a range of physiological pediatric hematocrits.

Methods

Geometric Model

A pediatric patient's aorta (8 years old) is reconstructed using magnetic resonance imaging (NIH-Georgia Tech Fontan Anatomy Database ID: CHOP007) and scaled down to represent a one year old pediatric patient with an aortic inlet diameter of 11.6 mm (Fig. 1A). All of the dimensions of the aortic model are within the range of morphological measurements previously reported by Machii and Becker [39]. Each branch vessel is extended ten times its diameter to allow the branch inlet flows to be independent of the outlet boundary conditions. To represent the outlet graft of a PVAD, a curved pipe with an internal diameter of 6 mm is attached to the ascending aorta in an end-to-side anastomosis (Fig. 1B). The 6 mm graft size fits pediatric patients from 0-12 months, weighing 2-8 kg [40]. Specific features of the cannula outflow graft and the end-to-side anastomosis discussed in this study are presented in Fig. 1C.

Viscoelastic Model

A viscoelastic blood model designed specifically for pediatric blood was previously used in a healthy pediatric ascending aorta model [38]. The generalized Oldroyd-B (GOB) model is based on a thermodynamic framework for non-linear rate type fluids developed by Rajagopal and Srinivasa [41]. In brief, the model uses the continuity and momentum equations (Eqs. 1, 2), splitting the viscous stress tensor into a solvent component (representing the Newtonian blood plasma) (Eq. 3) and a polymeric component (representing the viscoelastic RBCs). The polymeric stress component is modeled with a

neo-Hookean elastic response and a dissipative response that is quadratic in the stretch tensor. (Eqs. 4, 5).

$$\nabla \cdot u = 0 \quad (\text{Eq. 1})$$

$$\rho \frac{\partial u}{\partial t} + \rho u \cdot \nabla u = -\nabla p + \nabla \cdot (\tau_s + \tau_p) \quad (\text{Eq. 2})$$

$$\tau_s = 2\eta_\infty D \quad (\text{Eq. 3})$$

$$\tau_p + \frac{\eta}{2\mu} \overset{\sim}{\tau}_p + \alpha \frac{2\mu}{\eta} (\tau_p \cdot \tau_p) = \mu \lambda I \quad (\text{Eq. 4})$$

$$\lambda = \frac{3}{\text{tr}(B^{-1})} \quad (\text{Eq. 5})$$

Where u is the fluid velocity vector, ρ is the fluid density, p is the pressure, τ is the total viscous stress tensor composed of both the solvent (τ_s) and polymeric (τ_p) parts, η_∞ is the solvent viscosity, D is the symmetric part of the velocity gradient, η is the polymeric viscosity, μ is the elastic shear modulus, α is the Giesekus mobility parameter, λ is the relaxation time, B is the left Cauchy stretch tensor, and $\overset{\sim}{\tau}_p$ is the upper-convected time derivative (or Oldroyd derivative) of the polymeric stress.

The GOB model coefficients were found previously [38] from a least squares regression fit to pediatric viscosity versus shear rate data of patients from 4 days to 7.7 years old [30]. Three distinct GOB models were developed to fit pediatric hematocrit data of 20, 40 and 60%, representing the wide range of physiological hematocrit in neonate and pediatric patients.

Hemodynamic Parameters

The generation of pulsatility is dependent on the energy gradient and not just the pressure gradient [42, 43]. Therefore, to compare between the pulsatile and continuous PVAD flow modes, the surplus hemodynamic energy (SHE, ergs/cm³) (Eq. 6) is used.

$$SHE = 1332(EEP - TAP) \quad (\text{Eq. 6})$$

SHE is a measure of the extra energy generated from a flow pulsation and has previously been used to compare pulsatility in normal and heart failure patients [44], in PVADs in mock circulatory loops [45] and in computational fluid dynamics (CFD) studies on pulsatile and continuous CPB [27] among others. EEP and TAP are the energy equivalent pressure (mmHg) and time-averaged pressure (mmHg) defined by Eqs. 7 and 8, respectively.

$$EEP = \frac{\int_0^T p \cdot Q \cdot dt}{\int_0^T Q \cdot dt} \quad (\text{Eq. 7})$$

$$TAP = \int_0^T p \cdot dt \quad (\text{Eq. 8})$$

EEP is a ratio of the area beneath the hemodynamic power curve to the area beneath the pump flow curve during each pulse cycle. Q is the pump flow rate in liters per minute and p is the inlet/outlet boundary pressure in mmHg. SHE is then calculated by multiplying the difference between the EEP and TAP by the conversion factor 1332. For a purely steady flow, the EEP and TAP will be equal to each other resulting in a SHE of zero.

The hemodynamic parameters of WSS, TAWSS (Eq. 9) and OSI (Eq. 10) are important for vascular remodeling [21] and will be compared between the different flow modes and hematocrit models.

$$WSS_{Time-Averaged} = \frac{1}{T} \int_0^T WSS \cdot dt \quad (\text{Eq. 9})$$

$$OSI = \frac{1}{2} \left(1 - \frac{\left| \frac{1}{T} \int_0^T WSS \cdot dt \right|}{\frac{1}{T} \int_0^T |WSS| \cdot dt} \right) \quad (\text{Eq. 10})$$

Boundary Conditions

Three different inlet flow conditions are applied in this study (Table 1). Scaled plug flow velocity waveforms were acquired from an *in vivo* study of PVAD function in infant animal models [46] and scaled to represent a cardiac output (CO) of 1 L/min and a heart rate of 120 beats per minute (bpm). Case 1 represents a healthy pediatric aortic inflow (Fig. 2a) while Cases 2 and 3 represent 50% PVAD support in pulsatile and continuous operating modes, respectively. For the pulsatile flow mode (Case 2), scaled and synchronized waveforms are applied at both the inlet of the ascending aorta and the outlet of the cannula graft (Fig. 2b). For the continuous flow mode (Case 3), the same scaled waveform is applied at the ascending aorta inlet while a steady plug flow of 0.5 L/min is applied at the outlet of the cannula graft (Fig. 2c).

The outlets of the three aortic branch vessels and the descending aorta are given resistance boundary conditions for pressure (Eq. 11) to achieve physiological flow splitting:

$$p = RQ + p_0 \quad (\text{Eq. 11})$$

Where p is the pressure, Q is the flow rate, R is a resistance constant and p_0 is the aortic outlet pressure (assumed to be 60 mmHg [47]). For pediatric patients, 40-50% of cardiac output is diverted from the aortic arch into the branch vessels and flow in each respective branch vessel is proportional to its cross-sectional area [48]. Numerical studies were

performed to determine the correct resistance constant (R) at each outlet such that the total flow splitting into the vessels is 46.75%; 21.41%, 10.58% and 14.76% into the brachiocephalic, left common carotid and left subclavian arteries, respectively [26]. The resistance constants were found to be $2.4e^4$, $2.4e^5$, $3.6e^5$, and $1.8e^5$ Pa·s/m³ for the brachiocephalic artery, left common carotid artery, left subclavian artery and the aortic outlet, respectively, and were maintained for each simulation. Additionally, zero velocity gradient boundary conditions were applied at all outlets and no slip boundary conditions on all walls.

Grid Generation

High-quality unstructured grids have been generated using GAMBIT 2.3.16 (Fluent Inc., Lebanon, NH). Three grids (coarse ~ 180,000 cells; medium ~ 580,000 cells; and fine ~ 1,680,000 cells) were constructed for a systematic grid study. The heights of near-wall cells are approximately 0.5, 0.1, and 0.05 mm, respectively. The interior cells are a mixture of tetrahedral and hexahedral grids with nearly isotropic sizes of 1.0, 0.7, and 0.5 mm, respectively.

Flow Solver

OpenFOAM (OpenCFD Ltd), a C++ open-source CFD software that allows for user customized numerical solvers and pre- and post-processing utilities, is used in this study. A previously validated OpenFOAM solver for viscoelastic fluids developed by Favero *et al.* [49], viscoelasticFluidFoam, is used to solve the system of viscoelastic equations (Eqs. 1-6). In brief, viscoelasticFluidFoam takes the initial given fields and explicitly calculates the pressure gradient and stress divergence. Next, the momentum equation is implicitly solved for a new velocity field. The new velocity values are used to estimate a new pressure field and corrected using the pressure-implicit splitting operators (PISO) [50] scheme to satisfy continuity. Finally, a new stress tensor field is calculated using the chosen constitutive equation. For transient flows, this algorithm is iterated at each time step to achieve a desired accuracy.

The governing and constitutive equations are discretized using a finite volume method. The linear solvers used are a generalized geometric/algebraic multi-grid (GAMG) solver for pressure and a preconditioned bi-conjugate gradient (PBICG) solver for the velocity and stress tensors. A dynamic time-step control is used to maintain the Courant number under 1 throughout the entire cardiac cycle and the residuals of all variables are converged to 10^{-6} at every time step.

Results

Grid Sensitivity Analysis

A systematic grid study is performed on the pediatric aortic graft model to verify the numerical solutions (a previous grid study was performed on the healthy pediatric aorta model [38]). The pressures and volumetric flow rates at each of the inlets and outlets of the pediatric aortic graft model are measured throughout a full cardiac cycle of pulsatile PVAD support. Figure 3 shows pressure waveforms (mmHg) at each inlet and outlet boundary as a

function of time. All three grids show nearly identical results for both pressure and flow rate values. The largest differences in pressure occur during the flow reversal phase at the onset of diastole at the cannula and aortic inlets (Figs. 3a and 3b) between the coarse and fine grids (3 and 2% difference, respectively). No significant differences are observed at any boundary or time point between the medium and fine grids. Similar results were seen comparing the volumetric flow rates at the inlet and outlets with no differences seen between the medium and fine grids and are thus not included. The systolic and diastolic pressures are 87 and 56 mmHg, respectively, measured at the inlet of the aorta, and are well within physiological parameters for a 1 year old patient [47].

The effect of grid refinement on WSS at six locations along the length of the aortic wall was also investigated (Fig. 4). WSS is more sensitive to the grid compared to flow rate and pressure. Significant differences are seen prior to peak systole between the coarse grid and the medium and fine grids. The largest differences in WSS between the coarse and fine grid are 64%, 61% and 53% (Figs. 4a, 4b, and 4d, respectively). Between the medium and fine grids, the greatest difference in WSS is 15% just before peak systole (Fig. 4b). However, at all other time points in the cardiac cycle, excellent agreement is seen between the medium and fine grids with differences in WSS less than 6% at all locations. For these reasons, the medium grid is used for the remainder of the simulations.

Pulsatile Hemodynamic Performance

The pulsatile hemodynamic parameter of SHE is compared between the three flow conditions for each of the three hematocrit blood models at every inlet and outlet boundary (Table 2). Significant differences in vascular pulsatility are seen comparing each of the PVAD flow modes to the healthy flow mode (Fig. 5). Under pulsatile PVAD flow for the 40% hematocrit blood model, decreases in SHE of approximately 4%, 9%, 9% and 6% are seen at the brachiocephalic artery, left common carotid artery, left subclavian artery and aortic outlet, respectively. In comparison, much larger decreases of 84%, 85%, 84%, and 82% are seen at each of the same model outlets under continuous flow, respectively.

Pediatric hematocrit also plays a role in the pulsatile hemodynamic performance for all three flow conditions (Fig. 6). Comparing the lowest (20%) and highest (60%) hematocrit GOB blood models in this study, increases in SHE (between 3.4 and 4% depending on flow mode) are seen in the brachiocephalic artery with increasing hematocrit. Additionally, SHE increases are seen in both the left common carotid and left subclavian arteries with increasing hematocrit. In contrast, decreases in SHE (between 2.9 and 3.6% depending on flow mode) are seen at the aortic outlet with increasing hematocrit.

Comparison of Flow Modes

To identify the differences in flow fields between the three cases (healthy flow, 50% pulsatile PVAD flow and 50% continuous PVAD flow), the 40% hematocrit GOB blood model is studied at four time points throughout the cardiac cycle (Fig. 7). In the healthy case, blood flow is skewed toward the inner wall of the ascending aorta and outer walls around the aortic arch and into the descending aorta during systole (Fig. 7a). The highest velocity (2.08 m/s) occurs during peak systole in the descending aorta due to the tapering

geometry. Pulsatile PVAD flow leads to a high velocity jet into the ascending aorta during systole with flow skewed toward the outer wall of the ascending aorta (Fig. 7a). A peak velocity of 2.08 m/s is seen in the ascending aorta near the anastomotic toe with lower velocities in the descending aorta compared to the healthy case. The pulsatile PVAD jet also leads to higher velocities in the brachiocephalic artery (1.12 vs. 1.06 m/s) but lower velocities in the left subclavian artery (1.18 vs. 1.31 m/s). The continuous PVAD leads to a more uniform flow throughout the cardiac cycle but with higher velocities in the ascending aorta remaining into diastole due to the PVAD jet (Fig. 7a-d). A peak velocity of 1.36 m/s occurs during systole in the descending aorta. Flow remains in the aortic branch vessels throughout diastole (0.23 m/s) compared to extremely low velocity flow in both the healthy (0.01 m/s) and pulsatile PVAD (0.03 m/s) cases (Fig. 7d). Flow is also less skewed toward the outer wall at the end of the aortic arch in the descending aorta compared to both the healthy and pulsatile PVAD flows.

WSS is also compared between the three different flow modes with the 40% hematocrit GOB blood model at four time points throughout the cardiac cycle (Fig. 8). In the healthy aortic flow case, the maximum WSS is seen during peak systole between the left common carotid and left subclavian branches (685 dyne/cm²) (Fig. 8a). Additional high regions of WSS occur between the brachiocephalic and left common carotid branches and at the end of the aortic arch on the distal wall. The highest WSS for both PVAD flows occurs at the toe of the anastomosis with pulsatile flow resulting in an approximately 4 times higher WSS during peak systole (2345 vs. 615 dyne/cm²) (Fig. 8a). During diastole, however, much higher WSS is seen from continuous PVAD case (250 vs. 20 dyne/cm²) at the anastomosis toe compared to the pulsatile case (Fig. 8d). During systole, for both the healthy and pulsatile flow modes, high WSSs are seen between the brachiocephalic and left common carotid arteries and between the left common carotid and left subclavian arteries (Fig. 8a). During diastole, high WSSs are seen on both the inner and outer walls of the end of the aortic arch (Fig. 8d). Continuous PVAD flow results in high WSS between the left common carotid and left subclavian and on the proximal wall at the end of aortic arch throughout the entire cardiac cycle (Fig. 8a-d). During systole, these WSS values are much lower relative to the healthy and pulsatile PVAD cases but during diastole these WSS values are much higher.

TAWSS and OSI, important hemodynamic parameters of vascular remodeling, are compared between the three different flow modes with the 40% hematocrit GOB blood model (Fig. 9). Peak regions of TAWSS under healthy aortic flow occur between the aortic branches and on the distal end of the aortic arch (Fig. 9a). Similar high TAWSS regions are seen in both PVAD flow cases but the highest TAWSS occurs at the toe of anastomotic graft. The pulsatile PVAD TAWSS is higher at each of these peak locations compared to those with the continuous PVAD; at the anastomotic toe (525 vs. 345 dyne/cm²), between the brachiocephalic and left common carotid arteries (170 vs. 100 dyne/cm²), and on the distal end of the aortic arch (100 vs. 85 dyne/cm²). High regions of OSI, indicating flow separation and retrograde flow, in the healthy aortic case occur on the proximal walls of the aortic branch entrances and on the inner proximal wall of the aortic arch (Fig. 9b). Most of the aortic wall experiences low OSI with values less than 0.01 between the aortic branches and on the distal wall of the aortic arch. For both PVAD flow cases similar high and low

OSI regions are seen with additional high OSI areas just downstream of the anastomotic toe and on the anastomotic floor. The biggest difference between the two cases is the size and magnitude of high OSI region on the anastomosis floor. In the continuous PVAD case, OSI is much higher (0.48 vs. 0.35) and over a larger region compared to the pulsatile PVAD case due to the cannula inflow jet continuously impinging onto the floor throughout the cardiac cycle.

Comparison of Hematocrit Models

To investigate the effect of patient hematocrit on hemodynamics under healthy and PVAD aortic flow, differences in velocity (Fig. 10) and WSS (Fig. 11) are calculated between the 60% and 20% GOB blood models for all three flow cases at four different time points in the cardiac cycle. For the healthy flow case, higher velocities are seen with the 60% hematocrit compared to the 20% hematocrit during systole in the centers of the ascending (+0.06 m/s) and descending aorta (+0.05 m/s), brachiocephalic (+0.13 m/s), left common carotid and left subclavian arteries (+0.11 m/s) (Fig. 10a). Lower velocities are seen, however, with the 60% hematocrit around the walls of the ascending and descending aorta (-0.12 m/s) and on the posterior wall of the aortic arch (-0.29 m/s). At the onset of diastole (Fig. 10c), the 60% hematocrit also has significantly lower velocities in each of the aortic branches; -0.23 m/s in brachiocephalic artery and -0.1 m/s in the left subclavian and common carotid arteries.

Compared to the healthy flow case, both PVAD flow cases are less affected by hematocrit but with the pulsatile case seeing greater differences than the continuous case. For pulsatile PVAD flow at systole (Fig. 10a), the largest differences comparing the 60% to the 20% hematocrit are seen in the ascending (+0.14 m/s) and descending aorta (+0.07 m/s), brachiocephalic (+0.25 m/s) and left common carotid and subclavian arteries (+0.15 m/s). Lower velocities of -0.1, -0.23, and -0.31 m/s are seen at the walls of the ascending and descending aorta and on the posterior wall of the aortic arch. Additionally, velocities in the cannula are 0.11 m/s higher in the center with the 60% hematocrit but 0.12 m/s lower at the walls. Later in the cardiac cycle, at the onset of diastole (Fig. 10c), higher velocities are seen in the center of the descending aorta (+0.09 m/s) and left common carotid artery (+0.04 m/s) and lower velocities seen in the brachiocephalic and left subclavian arteries (-0.18 m/s) and at the wall of the descending aorta (-0.15 m/s). For the continuous PVAD case, higher velocities are seen with the 60% hematocrit in the ascending aorta, descending aorta and bypass graft (+0.04 m/s), in the brachiocephalic artery (+0.11 m/s) and in the left common carotid and subclavian arteries (+0.09 m/s) (Fig. 10a). Lower velocities are seen at the walls of the ascending (-0.04 m/s) and descending aortas (-0.16 m/s) and on the posterior wall of the aortic arch (-0.2 m/s). At the onset of diastole (Fig. 10c), higher velocities are seen in the center of the ascending aorta and bypass graft (+0.04 m/s), brachiocephalic (+0.03 m/s) and left subclavian artery (+0.07 m/s). Lower velocities are seen at the walls of the descending aorta (-0.12 m/s) and at points along the walls of the aortic branches (-0.09 m/s).

The range of pediatric patient hematocrit also has a significant effect on WSS for all flow modes and time points investigated (Fig. 11). For the healthy flow case, the biggest differences between the 60% and 20% hematocrit occur between the left subclavian and common carotid arteries and between the brachiocephalic and left common carotid arteries

with the 60% experiencing WSSs 405 and 355 dyne/cm² higher, respectively (Fig. 11a). In contrast, the inner wall of the aortic arch experiences lower WSS (-22 dyne/cm²) with the 60% hematocrit. Later in the cardiac cycle, at the onset of diastole (Fig. 11c), most of the model experiences lower WSS with the 60% hematocrit, including the proximal walls of the left common carotid and subclavian artery entrances (-40 dyne/cm²). The greatest differences for the 60% hematocrit case occur on both the distal and proximal walls of the end of the aortic arch into the descending aorta (+45 and +30 dyne/cm²). Each PVAD flow case is affected much differently by patient hematocrit both in location and magnitude of WSS difference. Both models experience the greatest difference at the toe of the anastomosis (1700 dyne/cm² higher with pulsatile support and 345 dyne/cm² higher with continuous support) (Fig. 11a). Compared to the healthy case, both PVAD flow cases see large WSS differences downstream of the toe (-60 and -15 dyne/cm²), on the proximal wall of the left subclavian entrance (-15 and -20 dyne/cm²) and on the inner wall of the aortic arch (-20 and -15 dyne/cm²). However, they did have the same regions of peak WSS differences with the 60% hematocrit model between the aortic branches (475 and 330 dyne/cm² with pulsatile PVAD and 155, 180 dyne/cm² with continuous PVAD). Later in the cardiac cycle the effect of hematocrit on WSS is greater for continuous flow compared to pulsatile flow. At the onset of diastole (Fig. 11c), peak WSS differences are still seen at the toe of the anastomosis with differences of 160 and 200 dyne/cm² in the pulsatile and continuous PVAD flows, respectively. Midway through diastole (Fig. 11d), WSS differences in the pulsatile case are between 7 and -5 dyne/cm² in the 60% hematocrit model but range between 35 and -5 dyne/cm² in the continuous case.

Discussion

Pulsatile Hemodynamic Performance

A previous study investigating pulsatility in healthy and heart failure adult patients found SHE values of approximately 2.1×10^4 ergs/cm³ in healthy patients, and 2×10^4 and 1.3×10^3 ergs/cm³ in patients under low flow pulsatile and continuous PVAD flow, respectively [44]. The differences in SHE found between the healthy baseline and pulsatile support cases were within 2.5% and not statistically significant. Another pulsatility study using CFD in a pediatric aorta with a Newtonian blood model found SHEs of 2.4×10^4 , 2×10^4 and 9×10^3 ergs/cm³ in healthy, pulsatile and continuous flows, respectively [27]. These results compare very well to SHE values found in this study. In the healthy pediatric case, SHE was found to vary between 2.2 and 2.6×10^4 ergs/cm³, depending on the particular blood model used. Under PVAD flow, SHE values varied between 2 and 2.4×10^4 ergs/cm³ with pulsatile support and between 8.8 and 10.3×10^3 ergs/cm³ with continuous support.

In an *in vivo* study of PVAD support in infant piglet models, it was shown that 3 times greater pulsatility was achieved under pulsatile bypass compared to continuous bypass [46]. In the previously discussed pediatric CFD study [27], pulsatility was 2 times greater at the aortic inlet with pulsatile support and between 3.3 and 4.1 times greater at the aortic branches and descending aorta. Again these results compare very well to the SHE values found in this study where pulsatility was 2.3 times greater at the aortic inlet and between 2.2 and 2.4 times greater at the aortic branches and descending aorta. Overall, greater pulsatility

is seen at all outlets with pulsatile support compared to continuous support, but with both cases leading to a decrease in pulsatility compared to the healthy case.

Comparison of Flow Modes

Results of the healthy aortic flow simulations compare well with previous numerical and computational studies [25, 26, 51]. During systole, flow is skewed towards the inner wall in the ascending aorta and the outer wall in the descending aorta. The flow in the aortic branches is skewed toward the distal walls throughout systole but towards the proximal walls during retrograde flow at the onset of diastole. WSS, TAWSS and OSI in the healthy aorta are also similar to previous studies. Areas of low TAWSS and high OSI are found on the proximal branch vessel walls and the inner wall of the aortic arch suggesting flow separation and retrograde flow in these regions. Previous peak values of WSS (650 dyne/cm²) were seen during peak systole between the brachiocephalic and left common carotid artery [26] and peak values of OSI (0.47 [26] and 0.45 [52]) on the proximal wall of the brachiocephalic and left common carotid arteries. In comparison, in this study, peak WSS of 685 dyne/cm² (Fig. 8a) and peak OSI of 0.43 (Fig. 9b) were seen at the same locations.

Little previous work has been done on aortic anastomotic flow, especially for pediatric patients. It has been shown that PVAD support introduces very different flow patterns throughout the aortic model. Similar to studies by Yang *et al.* using a Newtonian blood model, the presence of the PVAD cannula jet impinges onto the aortic floor opposite of the anastomosis site and directs more flow into the brachiocephalic artery [26]. Peak WSS and TAWSS in that pulsatile PVAD study were found to be 1800 dyne/cm² and 438 dyne/cm², respectively, at the toe of the anastomosis compared to values of 2345 dyne/cm² (Fig. 8a and Fig. 12a) and 525 dyne/cm² (Fig. 9a and Fig. 12b) at the same location in this work. Similarly, with continuous flow, the highest TAWSS was found previously to be 258 dyne/cm² [27] at the anastomotic toe compared to 345 dyne/cm² (Fig. 9a and Fig. 12b) in this study. Slightly larger WSS and TAWSS are to be expected comparing a viscoelastic blood model to a Newtonian model due to the increased effective viscosity of the blood that occurs during periods of low shear rate in diastole. More extensive work has been done on general end-to-side anastomosis models to understand the hemodynamics and potential sites of graft failure. In a photochromic tracer study of a 45° anastomosis junction, Ojha *et al.* found that under pulsatile flow WSS was near zero throughout the cycle at the heel and at the floor across from the heel of the anastomosis and that flow separation occurred just beyond the toe [53]. Similarly, for both pulsatile and continuous PVAD support in this study, WSS and TAWSS are seen to be near zero (Fig. 12a, b) at the heel and floor of the anastomosis.

Comparison of Hematocrit Models

Several previous studies have shown the wide variability in neonate and pediatric hematocrit. Jopling *et al.* found, analyzing patient data from a multi-hospital health care system, that hematocrit varied between 42 and 65% at birth [31]. Matoth *et al.* showed that hematocrit decreases with neonate age up to 12 weeks and can range from 60 down to 30% [29]. Long *et al.* analyzed data on patients ranging from 4 days to 7.7 years with a

hematocrit range of 19 to 56% and showed that different hematocrits had a strong influence on blood's resultant viscoelastic parameters [30]. Therefore, it is important to understand the differences in hemodynamics that can result from this hematocrit variability.

For the pulsatile PVAD case during peak systole, the differences in velocity in the ascending aorta and aortic branches are approximately 7 and 22% of the average velocity in those regions, respectively. For the continuous PVAD case, the differences in velocity in the descending aorta and aortic branches are approximately 12 and 10% of the average velocity in those regions, respectively. Similarly with WSS for both PVAD flows, peak WSS at the anastomotic toe nearly doubles from the 20 to 60% hematocrit; 1685 vs. 3340 dyne/cm² for pulsatile flow and 480 vs. 780 dyne/cm² for continuous flow. WSS between the left common carotid and left subclavian arteries also see significant increases from the 20 to 60% hematocrit models; 490 vs. 805 dyne/cm² for pulsatile flow and 245 vs. 410 dyne/cm² for continuous flow. A pronounced difference is still seen at the onset of diastole at the anastomotic toe under continuous support (220 vs. 380 dyne/cm²) but not under pulsatile support (75 vs. 90 dyne/cm²). Additionally, looking at TAWSS, even more dramatic differences are seen under both pulsatile (45 vs. 395 dyne/cm² at the toe and 14 vs. 100 dyne/cm² between the left common carotid and left subclavian arteries) and continuous (240 vs. 395 dyne/cm² at the toe and 70 vs. 115 dyne/cm² between the left common carotid and left subclavian arteries) support between the 20 and 60% hematocrit models. While the velocity field is strongly influenced by the pediatric hematocrit, WSS is more significantly affected in part due to its dependence on viscosity that increases with increasing hematocrit and with decreasing shear rate. To accurately study any pediatric blood flow application it is necessary to model the range of pediatric hematocrit due to the significant effect it has on WSS.

Implications for IT and Hemolysis

In a study correlating experimental WSS to *in vivo* IT in canine models, Loth *et al.* found an inverse correlation between WSS and IT for regions located on the juxta-anastomotic graft [54]. Additionally, several studies have suggested that regions of both low TAWSS (<4 dyne/cm²) [55] and high OSI (> 0.2) [56] are the most likely to develop IH due to the stimulation of an atherogenic phenotype in the endothelial cells. Looking at just the anastomosis site, regions of both low TAWSS and high OSI include the anterior wall downstream of the toe, the floor, and aortic wall upstream of the heel in both the pulsatile and continuous PVAD cases (Fig. 12b,c). Therefore, these regions may be prone to the development of IT in pediatric patients and eventual graft failure.

Looking at the potential for hemolysis in PVAD flow, previous work has shown that shear stresses of 1500 dyne/cm² [57] are enough to cause blood damage. In both the healthy flow and continuous PVAD flow cases this shear stress threshold is never reached but at peak systole with pulsatile PVAD support it is exceeded at the outlet of the PVAD cannula and anastomotic toe (2345 dyne/cm²) (Fig. 8a). This is similar to previous work by Pekkan *et al.* where they looked at blood damage in neonatal, pediatric and CPB aortic models and found that hemolysis only occurred during peak systole in the CPB model [25]. Additionally, in a study comparing the relative hemolysis in healthy and pulsatile and continuous PVAD

flows, it was found that pulsatile flow lead to an 18% increase while continuous flow lead to a 72% decrease in hemolysis compared to the healthy case [26]. Along with the WSS results in this study, it suggests that hemolysis is more of a concern during pulsatile PVAD support compared to continuous PVAD support due to the high velocity jet exiting the cannula at peak systole.

Limitations

This study uses a pediatric aortic model scaled to represent a 1 year old patient with all dimensions validated with existing morphological measurements by Machii and Becker [39]. However, both the diameters and lengths of different segments of the pediatric aorta can vary between patients and thus the effects of each PVAD flow mode and viscoelastic hematocrit model could lead to slightly different results. The aorta and PVAD cannula are both modeled with rigid walls, and therefore could lead to an over prediction of the SHE and overall pulsatility. An elastic wall model would likely damp out more of the pulsatility and decrease the SHE at each of the aortic outlets. However, the same trends seen comparing the different PVAD flow modes to the healthy baseline case would still likely hold.

Additionally, in both of the PVAD flow cases, a healthy aortic geometry is still used. To better improve the design of PVADs, both diseased state and surgically repaired aortic models should be studied in the future to more accurately see the effects of each flow mode.

Conclusions

This study examines hemodynamics in a pediatric aorta under healthy and both pulsatile and continuous PVAD flow conditions. Using a previously validated viscoelastic model designed specifically for pediatric blood, hemodynamic parameters of pulsatility, velocity, WSS, TAWSS and OSI are analyzed. It is shown that both pulsatile and continuous PVAD flow lead to a decrease in pulsatility (SHE, ergs/cm^3) compared to healthy aortic flow but with continuous PVAD pulsatility between 2.2 to 2.4 times lower than pulsatile PVAD pulsatility at each aortic outlet. Significant differences are also seen between the two PVAD flow modes in velocity and WSS. The higher velocity jet during systole with pulsatile flow leads to higher WSSs at the anastomotic toe and at the aortic branch bifurcations. The lower velocity but continuously flowing jet with continuous support leads to a much different flow field and higher WSSs into diastole. It was also shown that under a range of physiological pediatric hematocrit (20-60%) both velocity and WSS can vary significantly with the higher hematocrit blood model generally leading to higher peak WSSs but also lower WSSs in regions of flow separation. The large decrease in pulsatility seen from continuous PVAD support could lead to complications in pediatric organ development while the high WSSs during peak systole from pulsatile PVAD support could lead to blood damage. Both PVAD flow modes lead to similar regions prone to IH resulting from low TAWSS and high OSI.

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Fig. 1.

(a) A generalized pediatric aorta model (NIH-Georgia Tech Fontan Anatomy Database ID: CHOP007) scaled to represent a one year old patient. (b) Aortic model with an attached 6 mm diameter cannula graft via an end-to-side anastomosis. (c) Enlarged view of the graft end-to-side anastomosis

Fig. 2. (a) Healthy aortic inflow waveform, (b) pulsatile PVAD aortic and cannula waveforms and (c) continuous PVAD aortic and cannula waveforms

Fig. 3. Inlet and outlet boundary pressure values (mmHg) for three grids (coarse, medium and fine) over a single cardiac cycle

Fig. 4. WSS (dyne/cm^2) at six locations along the length of the aorta for three grids (coarse, medium and fine) over a single cardiac cycle

Fig. 5. Percent decrease in SHE (ergs/cm^3) at each outlet boundary from the healthy aortic flow to both the pulsatile and continuous PVAD flows

Fig. 6. Percent difference in SHE (ergs/cm³) from the 20% to the 60% hematocrit GOB models for all three flow modes

Fig. 7.

Velocity magnitude (m/s) comparison between the healthy aortic flow and pulsatile and continuous PVAD flows for the 40% hematocrit GOB model at four time points in the cardiac cycle ((a) peak systole, (b) mid-deceleration of systole, (c) onset of diastole and (d) mid-diastole). [Note the different velocity scales for each time point]

Fig. 8.

WSS magnitude (dynes/cm²) comparison between the healthy aortic flow and pulsatile and continuous PVAD flows for the 40% hematocrit GOB model at four time points in the cardiac cycle ((a) peak systole, (b) mid-deceleration of systole, (c) onset of diastole and (d) mid-diastole). [Note the different WSS scales for each time point]

Fig. 9. (a) TAWSS magnitude (dynes/cm²) and (b) OSI comparison between the healthy aortic flow and pulsatile and continuous PVAD flows for the 40% hematocrit GOB model. [Note the different TAWSS and OSI scales]

Fig. 10.

Differences in velocity magnitude (m/s) between the 60% and 20% hematocrit GOB models for the healthy aortic flow and pulsatile and continuous PVAD flows at four time points in the cardiac cycle ((a) peak systole, (b) mid-deceleration of systole, (c) onset of diastole and (d) mid-diastole). [Note the different velocity scales for each time point]

Fig. 11.

Differences in WSS magnitude (dynes/cm²) between the 60% and 20% hematocrit GOB models for the healthy aortic flow and pulsatile and continuous PVAD flows at four time points in the cardiac cycle ((a) peak systole, (b) mid-deceleration of systole, (c) onset of diastole and (d) mid-diastole). [Note the different WSS scales for each time point]

Fig. 12. (a) Peak WSS, (b) TAWSS and (c) OSI are compared between the pulsatile and continuous PVAD modes at the anastomosis site. [Note the different units and scales for each hemodynamic parameter]

Table 1

Healthy and PVAD Flow Conditions

Case	% Support	PVAD Mode	Heart Beat Rate (bpm)	Heart Flow Rate (L/min)	PVAD Beat Rate (bpm)	PVAD Flow Rate (L/min)
1	0	N/A	120	1.0	N/A	N/A
2	50	Pulsatile	120	0.5	120	0.5
3	50	Continuous	120	0.5	N/A	0.5

Table 2**Surplus Hemodynamic Energy (ergs/cm³) Results**

Blood Hematocrit	Flow Mode	Aortic Inlet	Cannula Outlet	Brachiocephalic	Left Common Carotid	Left Subclavian	Aortic Outlet
20%	Healthy	22129.28	N/A	19588.47	19341.69	17842.60	4815.17
20%	Pulsatile	20389.83	24914.23	18683.26	17600.68	16172.54	4508.06
20%	Continuous	8831.94	8879.60	7914.37	7744.88	7250.05	1997.94
40%	Healthy	23616.92	N/A	19810.87	17756.90	16260.37	4453.38
40%	Pulsatile	21858.00	27099.62	18996.86	17756.90	16260.37	4453.38
40%	Continuous	9390.76	9407.34	8045.16	7811.15	7276.15	1975.23
60%	Healthy	26077.40	N/A	20269.56	19657.45	17979.65	4644.73
60%	Pulsatile	24005.20	30343.15	19411.02	17942.34	16445.42	4374.41
60%	Continuous	10305.29	10283.56	8237.95	7900.18	7331.52	1940.68