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Asynchronous Pumping of a Pulsatile Ventricular Assist Device in a Pediatric Anastomosis Model

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Abstract

Background: Both pulsatile and continuous flow ventricular assist devices are being developed for pediatric congenital heart defect patients. Pulsatile devices are often operated asynchronously with the heart in either an “automatic” or a fixed beat rate mode. However, most studies have only investigated synchronized ejection.

Methods: A previously validated viscoelastic blood solver is used to investigate the parameters of pulsatility, power loss, and graft failure in a pediatric aortic anastomosis model.

Results: Pulsatility was highest with synchronized flow and lowest at a 90° phase shift. Power loss decreased at 90° and 180° phase shifts but increased at a 270° phase shift. Similar regions of potential intimal hyperplasia and graft failure were seen in all cases but with phase-shifted ejection leading to higher wall shear stress on the anastomotic floor and oscillatory shear index on the anastomotic toe.

Conclusion: The ranges of pulsatility and hemodynamics that can result clinically using asynchronous pulsatile devices were investigated in a pediatric anastomosis model. These results, along with the different postoperative benefits of pump modulation, can be used to design an optimal weaning protocol.

Keywords

pediatric; ventricular assist device; pulsatility; asynchronous; computational

Introduction

Congenital heart defects occur in approximately 1 in every 110 births in the United States,¹ with heart transplantation the only option for many. Additionally, in the United States, infants awaiting heart transplantation face the highest wait-list mortality in transplantation medicine, with 23% dying within six months of being listed for transplantation.² The use of

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mechanical circulatory support devices has been shown to decrease this high mortality rate and improve the efficiency of organ utilization in children.³ However, the only current options for pediatric and neonate patients are traditional extracorporeal membrane oxygenation, adult left ventricular assist devices (LVADs), and the Berlin Heart EXCOR pediatric VAD (PVAD).⁴ To address the lack of devices for pediatric patients, the Pediatric Circulatory Support Program was established to fund the development of a family of pediatric circulatory support devices.⁵

Compared to pulsatile volume-displacement LVADs, which can operate in a “full-to-empty” mode that automatically adjusts beat rate to changes in left ventricular preload,⁶ continuous flow LVADs are designed to operate at fixed rotational speeds that do not adjust to preload. There are also concerns over the level of pulsatility generated when using any LVAD and its effect on patient outcomes. Several studies have shown that pulsatile flow ventricular support improves blood flow to the brain and kidneys,⁷ heart,⁸ and liver⁹ in pediatric and neonate patients. To overcome the pulsatility deficit of continuous flow LVADs, previous investigators have studied the effects of modulating the devices’ rotational speeds to generate pulsatility in animal¹⁰ and computational models.¹¹ Early speed modulation strategies favored asynchronous control,¹² while more recent studies have implemented synchronous modulation control modes.¹³ With respect to both modulated continuous devices and naturally pulsatile devices, there is still discussion over the control type and synchronization with the patient’s native heartbeat. Left ventricular assist devices can be synchronized in either a copulsation or counterpulsation mode based on triggering from an acquired electrocardiogram (ECG) signal or unsynchronized based on a fixed or variable beat rate.

In the case of the Penn State pneumatic pulsatile PVAD, the pump is run in an asynchronous “full-to-empty” mode where the PVAD beat rate varies depending on filling from the left ventricle. This control mode has been shown to guarantee both complete filling of the device and complete washing of all blood-contacting surfaces for sac-type devices like the Penn State PVAD.¹⁴ Similarly, the Thoratec pulsatile VAD for adult patients, another sac-type pneumatic pump, is run in the full-to-empty mode to prevent thrombosis but can also be run at fixed beat rates or synchronously with an ECG signal.¹⁵ The Berlin Heart EXCOR, however, is run at a fixed beat rate that is determined under echocardiogram where complete filling and emptying are ideally achieved by adjusting the vacuum and ejection pressures.¹⁶

Another potential complication of PVAD use is the failure of the anastomotic graft due to intimal hyperplasia (IH) occurring in response to altered flow patterns and hemodynamics.¹⁷ Intimal hyperplasia in the anastomotic region of vascular grafts has been linked to several wall shear stress (WSS) parameters and oscillatory shear index (OSI) and shown to commonly occur at the heel, toe, and graft floor locations. Although IH has not been reported in PVAD patients, these parameters warrant study as areas of interest. Previous computational studies have compared the pulsatility and hemodynamics resulting from continuous and pulsatile flow support in a pediatric end-to-side anastomosis model,^{18,19} but under the assumption of synchronized copulsation of the heart and PVAD which is rarely the case for either the Penn State PVAD or Berlin Heart EXCOR. Therefore, to fully understand the pulsatility and hemodynamics that can occur clinically, a range of asynchronous beating

conditions need to be considered. This study will investigate the relationship between heart and PVAD ejection timing and its effect on pulsatility and hemodynamics in computational fluid dynamics simulations of a pediatric anastomotic graft model using a viscoelastic blood model.

Materials and Methods

Computational Model

An eight-year-old healthy patient's aorta was reconstructed using magnetic resonance imaging (NIH-Georgia Tech Fontan Database ID: CHOP007) and scaled down to represent a one-year-old pediatric patient with an aortic inlet diameter of 11.6 mm (Figure 1A). All dimensions of the aortic model were scaled accordingly and were within the range of reported morphological measurements.²⁰ To represent the PVAD outlet graft, a 6-mm-diameter curved pipe (fits patients 0–12 months weighing 2–8 kg)²¹ was attached to the ascending aorta in an end-to-side anastomosis configuration (Figure 1B).

Three high-quality unstructured grids were constructed using GAMBIT 2.3.16 (coarse ~180,000 cells; medium ~580,000 cells; fine ~1,680,000 cells). The grids were a mixture of tetrahedral and hexahedral cells with nearly isotropic sizes of 1.0, 0.7, and 0.5 mm, respectively. A systematic grid study was previously performed on the pediatric anastomosis model to verify the numerical solutions throughout a cardiac cycle,¹⁹ and the medium grid was chosen for all future simulations.

Viscoelastic Blood Model and Solver

A viscoelastic model designed for pediatric blood was previously developed and validated for different physiological hematocrits and was shown to predict velocities up to 30% higher in the aortic branches and peak WSSs 43% higher at the branch bifurcations compared to a standard Newtonian model.²² The generalized Oldroyd-B (GOB) model, based on a thermodynamic framework for nonlinear rate type fluids,²³ splits the viscous stress tensor of the momentum equation (Equation 1) into solvent (Newtonian blood plasma; Equation 2) and polymeric (viscoelastic red blood cell) components (Equations 3 and 4):

$$\rho \frac{\partial u}{\partial t} + \rho u \cdot \nabla u = -\nabla p + \nabla \cdot (\tau_s + \tau_p), \quad (1)$$

$$\tau_s = 2 \eta_\infty D, \quad (2)$$

$$\tau_p + \frac{\eta}{2\mu} \ddot{\tau}_p + \alpha \frac{2\mu}{\eta} (\tau_p \cdot \tau_p) = \mu \lambda I, \quad (3)$$

$$\lambda = \frac{3}{tr(B^{-1})}, \quad (4)$$

where u is the velocity, ρ is the density, p is the pressure, τ is the viscous stress tensor with 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 modulus, α is the Giesekus mobility parameter, λ is the relaxation time, B is the left Cauchy stretch tensor, and $\tau \dot{p}$ is the Oldroyd derivative of the polymeric stress. The GOB model coefficients were found²² from a fit to pediatric viscosity versus shear rate data.²⁴ To represent the wide range of physiological pediatric hematocrit,^{24–26} three sets of coefficients were found from fitting to 20%, 40%, and 60% hematocrit data. For this work, only the 40% hematocrit model was used ($\mu = 5.3$ cP/s, $\eta_\infty = 4.45$ cP, and $\eta = 20$ cP).

OpenFOAM (OpenCFD Ltd) CFD 2.4.0 (Bracknell, United Kingdom) software was used in this study along with a previously validated finite-volume solver for viscoelastic fluids (“viscoelasticFluidFoam”).²⁷ A dynamic time step was used to maintain the Courant number under 1 throughout the entire cardiac cycle, and the residuals of all variables were converged to 10^{-6} at every time step.

Boundary Conditions

Plug flow velocity waveforms at the inlets of the ascending aorta and PVAD cannula were acquired from an in vivo study of PVAD function in infant animal models.²⁸ Both waveforms were scaled to 120 beats/min (bpm) and 0.5 L/min (total cardiac output of 1 L/min). In case 1, both waveforms were synchronized in a copulsation mode. In cases 2 to 4, to represent the range of asynchronous ejection of the Penn State pulsatile PVAD, the cannula inlet waveform was shifted 90°, 180° (counterpulsation), and 270° out of phase with respect to the aortic inlet waveform (Figure 1C).

The outlets of the aortic branches and descending aorta were given resistance boundary conditions for pressure (Equation 5) to achieve physiological flow splitting:

$$p = RQ + p_0, \quad (5)$$

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 mm Hg).²⁹ For pediatric patients, 40% to 50% of their cardiac output is diverted into the aortic branches, and flow into each branch is proportional to its cross-sectional area.³⁰ Numerical studies were performed to determine the correct resistance constants (R) such that the flow splitting was 21.41%, 10.58%, 14.76%, and 53.25% into the brachiocephalic, left common carotid, and left subclavian arteries, and descending aorta, respectively.³¹ Zero velocity gradient boundary conditions were applied at all outlets and no-slip boundary conditions on all walls.

Hemodynamic Parameters

To compare the pulsatility generated from each flow condition, both the pulse pressure and surplus hemodynamic energy (SHE)³² were calculated at each of the aortic outlets. The pulse pressure, defined as the difference between the systolic and diastolic pressures, is often used clinically. Surplus hemodynamic energy, however, is a more accurate measure because the generation of pulsatility depends on an energy gradient and not just a pressure gradient. Surplus hemodynamic energy is defined as the extra energy generated from a flow pulsation (Equation 6), based on the difference between Shepard's energy equivalent pressure (EEP; Equation 7)³³ and the time-averaged pressure (TAP; Equation 8):

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

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

$$\text{TAP} = \frac{1}{T} \int_0^T p \cdot dt. \quad (8)$$

Although pulse pressure and SHE are indices of pulsatile performance, an additional parameter of power loss (p_{loss} ; Equation 9) was measured as an index of temporal pulsatile energy loss:

$$p_{\text{loss}} = \sum_{\text{inlets}} p \cdot Q - \sum_{\text{outlets}} p \cdot Q. \quad (9)$$

p_{loss} has previously been used in the design of cardiopulmonary bypass cannulas³⁴ and in predicting total cavopulmonary connection success.³⁵ Additionally, the hemodynamic parameters of WSS, time-averaged WSS (TAWSS; Equation 10), and OSI (Equation 11) are important for vascular remodeling and were also compared between the different flow conditions:

$$\text{TAWSS} = \frac{1}{T} \int_0^T \text{WSS} \cdot dt, \quad (10)$$

$$\text{OSI} = \frac{1}{2} \left(1 - \frac{\left| \frac{1}{T} \int_0^T \text{WWS} \cdot dt \right|}{\frac{1}{T} \int_0^T |\text{WWS}| \cdot dt} \right). \quad (11)$$

Results

Pulsatile Hemodynamic Performance

Due to the different timing of PVAD ejections, the aortic branches and descending aorta had large differences in their flow rate and pressure traces (Figure 2). The copulsation case led to large spikes in both flow rate and pressure early in the cardiac cycle due to the simultaneous ejection of the heart and PVAD. Peak values of 16.3 mL/s and 83.2 mm Hg were seen in flow rate and pressure, respectively, at the outlet of the brachiocephalic artery (Figure 2A). The phase-shifted PVAD flow cases resulted in two separate and lower magnitude spikes. For these three cases, all peak flow rates and pressures occurred during PVAD ejection and not during heart ejection. The lowest values at all outlets were in the 90° shifted case and increased with additional phase shift. Comparing the values for each phase-shifted flow in the brachiocephalic artery (Figure 2A), peak flow rates of 8.9, 9.2, and 10.6 mL/s and peak pressures of 72.8, 73.1, and 75.1 mm Hg were seen in the 90°, 180°, and 270° shifted flows, respectively. The lower velocities and pressures observed in the 90° phase-shifted flow were most likely due to backflow at the aortic inlet (Figure 1C) that occurred at approximately 0.18 seconds into the cardiac cycle, just as the PVAD was ejecting.

Two measures of pulsatility investigated in this study, pulse pressure and SHE, both showed the same trends between the different flow cases (Figure 3). Synchronized copulsation led to the highest pulsatility at the aortic outlets and the 90° phase lag led to the lowest pulsatility with additional PVAD lag leading to increases in pulsatility. Additionally, both pulsatility measures were the highest at the brachiocephalic artery and decreased with lateral distance (lowest pulsatility in the descending aorta). The differences in pulsatility were less pronounced between cases, however, with pulse pressure than with SHE. In the brachiocephalic artery, percentage decreases in pulse pressure of 43%, 34%, and 25% (Figure 3A) were observed in the copulsation case and each increasing phase shift, respectively. For SHE, these decreases were 68%, 64%, and 58% (Figure 3B) with increasing phase shift, respectively. Compared to the aortic branches, smaller pulsatility differences were observed in the descending aorta where both parameters showed nearly the same 60% decrease between the copulsation and phase-shifted flows.

The temporal changes in power loss showed similar trends to the flow and pressure waveforms in Figure 2 but with the PVAD ejection contributing more to the power loss compared to the heart ejection. The peak and average power losses were 154 and 25 mW, 64 and 13 mW, 68 and 12 mW, and 100 and 29 mW for the synchronized and phase-shifted cases, respectively.

Graft Flow Hemodynamics

Examining the flow fields at the anastomotic junction (Figure 4), it is clear that the impact of the PVAD cannula jet varied due to its ejection timing. The greatest differences occurred during peak ejections of the PVAD (Figure 4A) and heart (Figure 4B) in each simulation and were located at the anastomotic toe, floor, and heel (labeled 1, 2, and 3, respectively, in Figure 4A). Recirculation zones developed downstream of the anastomotic toe (region 1) in all cases during peak pump ejection (Figure 4B). However, the recirculation region was much larger in the phase-shifted cases compared to the synchronized case. Furthermore, the PVAD cannula jet impinged more onto the anastomotic floor (region 2) in the three shifted cases compared to the synchronized case where the interaction with the heart flow directed the jet downstream toward the aortic branches. The interaction between the heart and PVAD flow was also more significant during peak heart outflow (Figure 4A) for the synchronized case and led to higher velocities at the anastomotic toe (region 1) that were not observed in the other cases. With respect to all cases, low velocities were observed at the anastomotic heel (region 3) throughout the entire cardiac cycle.

Peak WSS occurred in all four cases at the anastomotic toe and at peak ejection of the PVAD. The highest WSS magnitude of 2,360 dyne/cm² occurred during copulsation, while the three phase-shifted cases showed similar peak WSSs of 1,839, 1,847, and 1,894 dyne/cm², respectively. A more important parameter for investigating long-term graft failure is TAWSS. Again, the location of greatest TAWSS in all cases was at the anastomotic toe and was greatest during copulsation (527 dyne/cm²; Figure 5A). Peak TAWSS for the phase-shifted flows were 432, 427, and 477 dyne/cm², respectively. Another important region with respect to graft failure and vascular remodeling is the floor of the anastomosis. At this location, TAWSS was significantly lower in the copulsation case (8 dyne/cm²) than in the phase-shifted cases (50, 54, and 48 dyne/cm², respectively). Additionally, a high region of TAWSS was seen in all cases between the brachiocephalic and left common carotid arteries (169–183 dyne/cm²; Figure 5A).

High regions of OSI present in all of the PVAD flow conditions included the anastomotic floor, downstream of the anastomotic toe, and between the aortic branches (Figure 5B). For the synchronized case, OSIs of 0.44 occurred downstream of the anastomosis on the anterior wall and 0.37 on the floor. For the phase-shifted flows at these same locations, OSIs of 0.48 and 0.44, 0.48 and 0.45, and 0.49 and 0.45 were observed for the 90°, 180°, and 270° shifts, respectively. High OSIs were also found in all cases on the proximal walls of the aortic bifurcations (0.45–0.47) and on the inner curvature of the distal aortic arch (0.42–0.45; Figure 5B).

Comment

Previous computational studies have investigated pulsatility under both pulsatile and continuous PVAD support but only during synchronized ejection of the heart and pump.^{18,19} However, due to the more common asynchronous pumping modes of pediatric devices, including the Penn State pneumatic PVAD and Berlin Heart EXCOR, it is important to study the pulsatility resulting from the full range of PVAD ejection timing that can occur clinically. Synchronized copulsation has previously been shown to decrease SHE approximately 15% compared to a healthy pediatric patient.¹⁹ However, with the PVAD pumping out of phase with the heart, the decreases in pulsatility compared to a healthy pediatric patient can decrease much more significantly. In the brachiocephalic artery, a 90° phase shift caused a 72% decrease in SHE, while the 180° and 270° phase shifts led to decreases of 73% and 65%, respectively. Additionally, continuous flow support has been shown to cause significant decreases in SHE compared to synchronized pulsatile support.¹⁹ However, when compared to the PVAD phase lag cases, the differences in SHE between pulsatile and continuous PVAD support were less pronounced (only 24%, 25%, and 41% higher in the brachiocephalic artery for 90°, 180°, and 270° phase shifts, respectively). Looking at average power loss, both the 90° and 180° shifts led to even greater power losses (49% and 52%, respectively) compared to the synchronized case, while the 270° shift led to an increase in power loss (15%). Additionally, compared to the power loss in previous simulations of a healthy pediatric patient and a patient under continuous PVAD support,¹⁹ there was little difference in average power loss between healthy and synchronized pulsatile flows (24 vs 25 mW), while continuous PVAD support led to a significant increase in power loss (110 mW) over all pulsatile flow cases.

To the authors' knowledge, no other experimental or computational studies have investigated the different synchronization and asynchronization modes of pulsatile VADs despite the prominence of these devices for pediatric patients. The majority of VAD timing studies have instead focused on adult continuous flow devices and their potential to generate pulsatility using rotational speed modulation techniques. Soucy et al¹⁰ studied the effect of modulation algorithms with the HeartWare HVAD centrifugal pump in a bovine model. Although the HeartWare's pulsatility was generated differently, similar trends in pulse pressure and SHE were seen to those in this work. Both pulsatility measures increased over baseline continuous support with any type of modulation. Similar to the copulsation and counterpulsation cases in this study, it was shown that operating the HVAD with 0° modulation phase shift generated greater pulsatility than with a 180° shift. Ising et al¹¹ studied the effects of continuous flow LVAD modulation in an adult lumped parameter model with different combinations of pulse widths, frequencies, and shifts. The baseline pulse pressure under 50% continuous flow support was 15 mm Hg, which is very similar to our previous work where pulse pressures of 14 mm Hg were measured under continuous support.¹⁹ Under synchronous pulsatile support, pulse pressures ranged between 14 and 21 mm Hg; and under asynchronous pulsatile support, pulse pressures ranged between 18 and 26 mm Hg. Although this study's beat rate (120 bpm) was higher than that of Ising et al¹¹ (20–80 bpm), the pulse pressures measured at each phase shift were still within their range (12–15, 14–17, and 16–19 mm Hg for 90°, 180°, and 270° cases, respectively; Figure 3A).

Similar to both Soucy et al and Ising et al, this study showed that copulsation generates higher pulsatility compared to any other asynchronous timing.

Wall shear stress, TAWSS, and OSI have all been shown to be important hemodynamic parameters of long-term graft durability and vascular remodeling. The critical regions of high WSS and TAWSS and both high and low OSI seen in this study were similar to previous computational models of aortic-anastomotic flows. Nearly identical peak WSS and TAWSS (1,800 and 438 dyne/cm², respectively) occurred at the toe of the anastomosis as reported by Yang et al¹⁸ in a PVAD anastomotic model compared to WSS values between 1,839 and 1,894 dyne/cm² and TAWSS between 427 and 477 dyne/cm² for all phase shifts in this study (Figure 5A). Sottiurai et al, in studies of polytetrafluoroethylene femoral grafts in dogs, found that IH was most common at the heel, toe, and floor of the anastomosis.³⁶ Other studies have suggested that regions of both low TAWSS (<4 dyne/cm²)³⁷ and high OSI (>0.2)³⁸ are most likely to develop IH due to the stimulation of an atherogenic phenotype in the endothelial cells. The same regions of both low TAWSS and high OSI were observed in all the phase-shifted flows: the anterior aortic wall downstream of the toe, the anastomotic floor, and the aortic wall upstream of the heel (Figure 5A and B). In the phase-shifted flows, higher WSS occurred on the anastomotic floor and higher OSI on the anastomotic toe compared to the synchronized case.

In a review of different modulation strategies of *in silico*, *in vitro*, and *in vivo* animal studies, Amacher et al¹³ showed that it may be beneficial to change the modulation throughout the postoperative recovery period. They showed that maximum left ventricular unloading was achieved at PVAD phase shifts of approximately 80%, maximum flow through the aortic valve was achieved at PVAD phase shifts of 50% to 60%, and the most physiological pulsatility was generated at PVAD phase shifts of 30%. Therefore, a higher phase shift early postoperatively with gradual reloading of the ventricle by changing the phase shift could be used as a weaning procedure. The pulsatility and hemodynamic results from this study, covering the range of possible PVAD phase shifts that would be prescribed under such a weaning protocol, can be used to help clinicians better optimize the procedure.

Limitations

The pediatric aorta was modeled with rigid walls in all simulations. The effect of aortic wall elasticity would most likely dampen the pressure spikes that occur due to heart and PVAD ejections and therefore decrease the overall pulsatility measures. However, the same trends between the different PVAD flow modes would likely still hold. This study also prescribed the upstream behaviors of the heart and PVAD with acquired *in vivo* boundary conditions and thus the heart and PVAD were unable to adapt to each other's behavior as they would clinically.

Conclusions

The ranges of hemodynamics that can result clinically using asynchronous pulsatile PVADs were investigated in a pediatric anastomosis model. Pulsatility, power loss, and graft failure parameters were compared between four different PVAD and heart ejection timings.

Pulsatility was highest in with synchronized flow and lowest at a 90° phase shift. Power loss decreased at 90° and 180° phase shifts but increased at a 270° phase shift. Similar regions of potential IH and graft failure were seen in all flow cases but with phase-shifted PVAD ejection leading to higher WSS on the anastomotic floor and OSI on the anastomotic toe. These results, along with the different postoperative benefits of pump modulation,¹³ can be used to design an optimal weaning protocol.

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Abbreviations and Acronyms

ECG	electrocardiogram
EEP	energy equivalent pressure
GOB	generalized Oldroyd-B
IH	intimal hyperplasia
LVAD	left ventricular assist devices
OSI	oscillatory shear index
PVAD	pediatric ventricular assist devices
SHE	surplus hemodynamic energy
TAP	time-averaged pressure
TAWSS	time-averaged wall shear stress
WSS	wall shear stress

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Figure 1.

A, Pediatric aortic model with attached pediatric ventricular assist device (PVAD) cannula.

B, Enlarged view of the graft end-to-side anastomosis. C, Pulsatile heart and PVAD velocity inlet waveforms.

Figure 2.

Flow rate (mL/s) and pressure (mm Hg) traces in the brachiocephalic artery, left common carotid artery, left subclavian artery, and descending aorta for the synchronized and three asynchronous cases.

Figure 3.

Comparison of (A) pulse pressure (mm Hg) and (B) SHE (ergs/cm³) in the brachiocephalic artery, left common carotid artery, left subclavian artery, and descending aorta for the synchronized and three asynchronous cases.

Figure 4. Velocity flow field (m/s) comparison in the ascending aorta during each respective cases (A) peak pediatric ventricular assist device (PVAD) and (B) heart ejections.

Figure 5.

(A) Time-averaged wall shear stress (TAWSS; dyne/cm²) and (B) oscillatory shear index (OSI) at the end-to-side anastomosis for the synchronized and three asynchronous cases.