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In Vitro Evaluation of Right Ventricular Outflow Tract Reconstruction With Bicuspid Valved Polytetrafluoroethylene Conduit

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Abstract: Conduits available for right ventricular outflow tract (RVOT) reconstruction eventually become stenotic and/or insufficient due to calcification. In order to reduce the incidence of reoperations we have developed and used a bicuspid valved polytetrafluoroethylene (PTFE) conduit for the RVOT reconstruction. The purpose of this study is to investigate the hemodynamic performance of the new design using a pediatric in vitro right heart mock loop. PTFE conduit has been used for the complete biventricular repair of 20 patients (age 1.7 ± 6 years) with cyanotic congenital defects. To account for the large variability of conduit sizes, 14, 16, 22, and 24-mm conduit sizes were evaluated using in vitro flow loop comprised of a pulsatile pump with cardiac output (CO) of 1.2–3.2 LPM, bicuspid valved RVOT conduit, pulmonary artery, venous compartments, and the flow visualization setup. We recorded the diastolic valve leakage and pre- and post-conduit pressures in static and pulsatile settings. In vitro valve function and overall hemodynamic performance was evaluated using high-speed cameras and ultrasonic flow probes. Three-dimensional flow fields for different in vivo conduit curvatures and inflow regimes were calculated by computational fluid dynamics (CFD) analysis to further aid the conduit design process. The average pressure drop over the valved conduits was 0.8 ± 1.7 mm Hg for the CO range tested. Typical values for regurgitant fraction, peak-to-peak pressure gradient, and effective office area were 23 ± 2.1%, 13 ± 2.4 mm Hg, and 1.56 ± 0.2 cm^2, respectively. High-speed videos captured the intact valve motion with asymmetrical valve opening during the systole. CFD simulations demonstrated the flow skewness toward the major curvature of the conduit based on the pulmonic curvature. In vitro evaluation of the bicuspid valved PTFE conduit coincides well with acceptable early clinical performance (mild insufficiency), with relatively low pressure drop, and intact valve motion independent from the conduit curvature, orientation or valve location, but at the expense of increased diastolic flow regurgitation. These findings benchmark the baseline performance of the bicuspid valved conduit and will be used for future designs to improve valve competency. **Key Words:** Heart valve—Congenital heart disease—Right ventricle outflow track reconstruction—Bicuspid valved conduit—Pulmonary valve—In vitro experimentation—Computational fluid dynamics—Hemodynamics/physiology—Regurgitant fraction.

Conduit selection for right ventricle outflow tract (RVOT) reconstruction presents a major challenge in the treatment of many congenital heart diseases (1) and in autograft pulmonary valve substitution, that is, Ross procedure (2). Bioprosthetic conduits available for RVOT reconstruction, that is, both xenografts and homografts, are insufficient due to poor hemodynamic performance and long-term complications associated with thrombosis and calcification, especially in very young patients (3–5). Replacement of the bioprosthetic valve is required when the individual reaches late adolescence or early adulthood. Mechanical

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valves have higher longevity but require aggressive anticoagulant therapy and pose a higher risk of thrombosis in the pulmonary position compared with left heart implantation (6,7). Lack of ideal conduit and the increasing need for valved conduits (especially at smaller diameters) demand alternative options.

To expand current conduit alternatives and to reduce the incidence of reoperation, we have developed and utilized a valved polytetrafluoroethylene (PTFE) conduit using standard stretch PTFE graft and 0.1 mm-thick PTFE membrane (WL Gore & Associates, Inc, Flagstaff, AZ, USA) for the reconstruction of the RVOT. Utility of PTFE has been previously demonstrated in monocuspid (8) and tricuspid (9) valved RVOT reconstruction with no significant calcification in any cases. Our preliminary clinical data indicated an acceptable early performance level with a low incidence of valve insufficiency and no conduit stenosis (10).

In vitro set-ups for testing prostatic valve performance focus primarily on the left heart hemodynamics to evaluate aortic valve replacements. Whereas, pulmonary arterial pressures and impedances are significantly lower than those in the left heart, which will affect the valve performance. Among the few published right heart (right ventricle [RV]) models, Gohean et al. (11) and Camp et al. (12) evaluated different aortic mechanical valves in the pulmonary position. Their results indicated aberrant valve closure for lower pulmonary impedance, which was related to their suboptimal in vivo performance. In contrast to mechanical valves and aortic root reconstructs, the performance of conduit-mounted synthetic valves has been investigated solely in clinical settings, according to our knowledge. To evaluate alternative valved conduit designs, a reliable bench-top pulsatile right heart model, which can produce a realistic local hemodynamic environment, is required.

The purpose of this study is to investigate the hemodynamic performance of the new design using in vitro experimentation coupled with numerical modeling of the RVOT conduit. The effect of the pulmonic curvature on local hemodynamics inside the "curved" conduit is investigated using computational fluid dynamics (CFD). Effect of several geometric parameters such as conduit curvature, location of the valve, and conduit orientation on the bicuspid valve competency is investigated using a pediatric in vitro right heart mock-up loop. The core objective of this study is to establish the baseline performance parameters for the bicuspid valve design in pulmonary position.

MATERIALS AND METHODS

Patient selection

Since October 2008 to September 2009, we have implanted bicuspid valved PTFE conduits in 20 patients with a median age of 1.7 years (6 days–16 years). Their diagnoses include: tetralogy of Fallot with pulmonary atresia in 10 patients, truncus arteriosus in 6 patients, congenital aortic stenosis in 2 patients, transposition of great arteries in 1 patient, and interrupted aortic arch with a ventricular septal defect in 1 patient. In 18 patients, a complete biventricular repair was performed. In the other two cases, the conduit was used for palliative right ventricular outflow reconstruction. The conduit sizes varied from 10 to 24 mm in diameter based on the patient body weight (10).

Mock circulation loop

The bench-top pediatric right heart circulation is comprised of (i) an RV chamber, that is, a silicon membrane bulb-shaped chamber within a fluid filled outer-chamber; (ii) a positive displacement pump to actuate the ventricle chamber; (iii) the bicuspid valved RVOT conduit; (iv) the flow visualization setup; (v) the variable resistance flow clamps and trapped air compliance chambers to set the pulmonary vascular impedance; (vi) a tricuspid valve before the ventricle chamber; (vii) a pulmonic head tank to set the diastolic pressure level; (viii) a static head pump; and (ix) an atrial head tank to ensure adequate filling to the ventricle during diastole, as shown in Fig. 1. Pulmonary impedance is adjusted based on the clinical catheter data from single ventricle patients (13) and summarized in Table 1. Ventricle chamber was driven by a positive displacement pulse duplicator (Harvard Apparatus, Holliston, MA, USA) with variable stroke volume (20–100 mL), heart rate (80–100 bpm), and ejection fraction (EF). In order to visualize the valve motion, a transparent bifurcation cell with borosilicate walls and optical flat ends was placed after the conduit.

Pressure measurements were performed before and after the conduit, at the ventricle and compliance chambers, yielding five simultaneous pressure measurements using TruWave disposable pressure transducers (Edwards Life Sciences, Irvine, CA, USA) attached to a multichannel differential amplifier (WPI Inc., Sarasota, FL, USA) in full bridge configuration. Flow rate through each tubing segment was measured using transonic flow probes (6XL and 9XL, Transonic Inc., Ithaca, MA, USA). A dedicated data acquisition module NI USB-6229 (NI Inc., Austin, TX, USA) with 16-bit resolution and

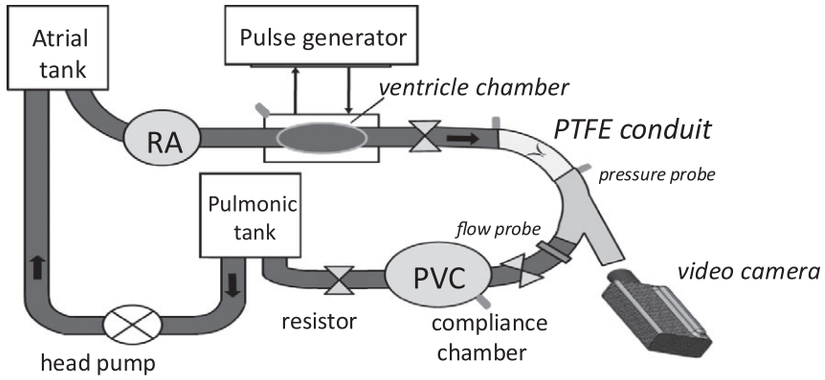

FIG. 1. Schematic representation of the pulmonary circulation mock loop bicuspid valved PTFE conduit attached to RV outflow. The in vitro flow loop was comprised of (i) RV chamber; (ii) positive displacement pump; (iii) the bicuspid valved RVOT conduit; (iv) flow visualization setup; (v) pulmonary resistance elements and compliance chambers; (vi) tricuspid valve before the ventricle chamber; (vii) pulmonic head tank; (viii) static head pump; and (ix) atrial head tank. The compliance chambers are represented by the ellipses. The double triangles, slender rectangles and small rectangles represent the flow resistors, velocity, and pressure measurement ports, respectively.

multiplexing capabilities was employed for sampling and recording data at 100 Hz. Distilled water ($\rho = 998$ kg/m^3) was used as the working fluid. Details of the compartment characterization are described previously by Dur et al. (14)

Experimental procedure

To account for the large variability of conduit sizes, four conduit diameter sizes—14 mm (C14), 16 mm (C16), 22 mm (C22), and 24 mm (C24)—were evaluated using the in vitro flow loop. The diastolic valve leakage was recorded under constant diastolic hydrostatic pressure gradient (ΔP) at four physiological pressure levels ($\Delta P = 5$, 10, 15, and 20 mm Hg). Pre- and postconduit (pulmonary artery [PA]), and ventricle pressures and flow were recorded in pulsatile settings. Pediatric EF was set to 45% (15) and cardiac output (CO) was adjusted between 1.2 and 3.2 LPM depending on the conduit size (10). Each conduit was analyzed under the same pulmonary vascular impedance. In vitro valve function and overall hemodynamic performance was evaluated using high-speed cameras and ultrasonic flow probes. The transparent cell and the camera were aligned with the conduit curvature to acquire the valve motion as shown in Fig. 2a.

Geometric effects were evaluated by comparing the valve competency when the conduit was oriented: (i) at the pulmonic curvature in comparison to the straight conduit; (ii) such that valve was located at the upstream, medial, and distal site along the conduit curvature; and (iii) similar to the anatomical orientation, that is, upright with an anterior to posterior curvature as shown in Fig. 2b. The conduit curvature was set based on the typical anatomical orientation of the RVOT conduit with a radius of curvature, R = 8. 2 cm, which corresponds to 70 degrees offset between the inlet and the outlet of the conduit. Conduits were oriented such that the missing lower cusp lies on the lower curvature. Performance of the different conduit designs were evaluated based on regurgitant fraction (RF), peak-to-peak transvalvular pressure gradient (PPG), and effective orifice area (EAO) (12), which are defined below.

TABLE 1. *Vascular parameters of the mock system simulating pulmonary circulation*

Parameter	Pulmonary circulation impedance
C_{RV}	0.4
C_{LA}	10
C_{PAVB}	10
R_{PAB}	1.4
R_{PVB}	1.1

Shown are the parameters implemented on the mock loop. Parameters are taken from patient data presented in Sundareswaran et al. (13).

C, compliance (mL/mmHg); R, resistance (mmHg L/min); LA, left atria; PAB, pulmonary arterial bed; PVB, pulmonary venous bed; PAVB, combined PA–venous bed.

$$RF = \frac{Q_{regurgitate}}{Q_{anterograde}} \quad (1)$$

$$PPG = RVP_{peak} - PAP_{peak} \quad (2)$$

$$EAO = \frac{Q_{rms}}{49.92\sqrt{\Delta P}} \quad (3)$$

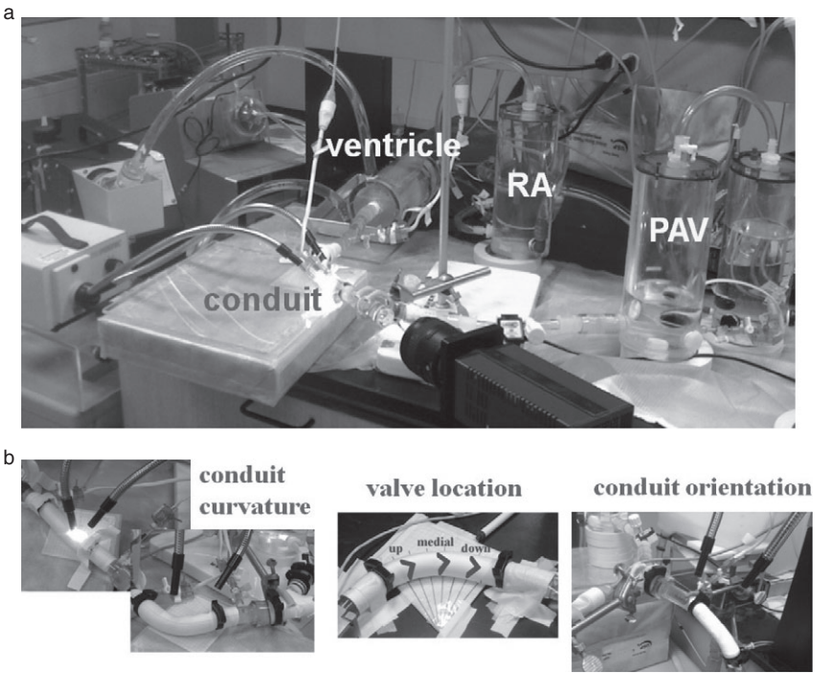

FIG. 2. In vitro pulmonary circulation flow loop shown during data acquisition (a). Valve motion is recorded using a camera placed downstream of the transparent bifurcation. Effect of conduit curvature, valve location, and conduit orientation on valve competency is evaluated (b).

Regurgitate and anterograde flows are calculated using the instantaneous flow waveforms. PPG is defined as the difference of peak RV and PA pressure pulse. Based on blood analog fluid assumption, EAO was estimated using root-mean-square flow rate (Q_{rms}) and mean systolic-to-diastolic pressure drop. Performance parameters were reported based on the time-averaging over 15 cycles and the ±values refer to the combined 85% uncertainty intervals.

Computational fluid dynamics

The three-dimensional flow fields for different in vivo conduit curvatures and inflow regimes were calculated by CFD analysis to further aid the conduit design process. Pulsatile blood flow was simulated inside the curved RVOT conduit using the second-order accurate CFD solver (FLUENT 6.3.26. ANSYS Inc., Canonsburg, PA, USA), which was originally developed for investigating the reconstructive surgeries for single ventricle palliation (16,17). Two conduits, C14 and C22, were evaluated based on the body surface area (0.5 and 1.35 m^2, respectively) and the corresponding COs (1.2 and 3.2 L/min, respectively). Analogous to the experiment settings, the baseline and smaller curvature were analyzed. Blood was chosen as Newtonian fluid with a viscosity of 3.71×10^{-3} N s/m^2 and a density of 1060 kg/m^3. Flow waveforms measured using the in vitro setup for the corresponding conduits and blunt flow profile (typical for ventricle) was assigned at the inlet of the conduit. Computational domain of each conduit design was discretized using 100 000 tetrahedral elements.

RESULTS

In vitro performance of bicuspid valved conduit

The bicuspid valved conduit reconstructed RVOT experiments produced physiological pulsatile flow and pressure waveforms in pulmonary circulation in agreement with the clinical data (18). RV and PA flow and pressure pulses measured at the pre- and postconduit sites for the pulmonic curvature of C16 (at the medial valve location) are shown in Fig. 3. Characteristic dicrotic notch, phase-lag between flow and pressure waveforms, and diastolic flow regurgitation are clearly visible in the PA pulse traces. Crossover of RV and PA pressure signals leads the onset of flow regurgitation.

Based on the static measurements, pressure drop across the valved conduit was calculated as 0.8 ± 1.7 mm Hg for all conduit sizes, which appears considerably lower than the echocardiography-derived values reported previously (10). Pressure drop across the conduit was essentially insensitive to valve location or the curvature of the conduit. Leakage flow measured during the complete closure of bicuspid valve was increased with the increasing diastolic

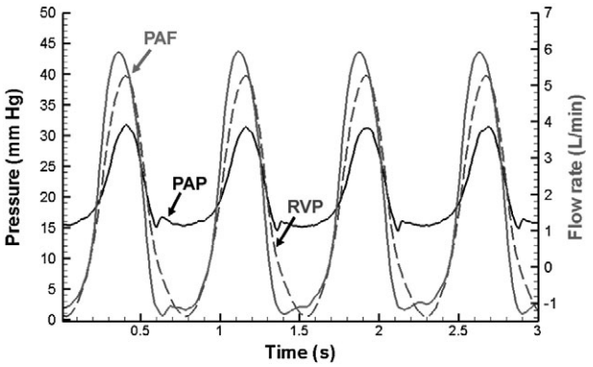

FIG. 3. Physiological PA flow (PAF) and pressure (PAP) waveforms and RV pressure (RVP) recorded at 1.5 L/min CO within conduit with 16 mm (C16) oriented in pulmonic curvature, that is, R = 8.2 cm, placed at the medial location along the curvature.

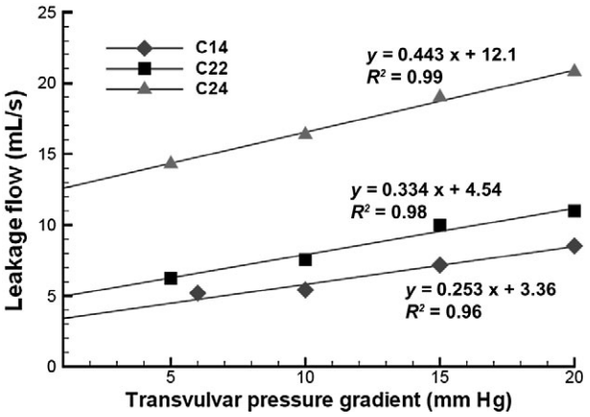

FIG. 4. Leakage flow across the fully closed bicuspid valve for four constant diastolic pressure gradients evaluated for conduits with diameters 14 mm (C14), 22 mm (C22), and 24 mm (C24). Mean leakage flow was calculated to be 0.34 ± 0.1 L/min/mm Hg.

pressure gradient as shown in Fig. 4. Diastolic valve regurgitation based on static transvulvar pressure gradient was calculated to be 0.34 ± 0.1 L/min/mm Hg. Diastolic valve regurgitation was higher for larger the size of the conduit.

High-speed videos captured the diastolic valve closure and asymmetrical valve opening, which indicated the unbalanced opening forces on leaflets during the systole (Fig. 5). An important surgical consideration for the design of the conduit-mounted valves is to assess the optimum valve location within the conduit. Results summarized in Table 2 show that the baseline RF, PPG, and EAO for C16 were 23 ± 2.1%, 13 ± 2.4 mm Hg, and 1.56 ± 0.2 cm^2. Distal valve location size was favored due to slightly decreased RF and increased EAO. There was no statistically significant relation between valve location or valve curvature and any of the performance parameters for bicuspid valve design. PPG increased by 23 ± 20% and EAO decreased by 3.9 ± 4.1% in the anatomical upright conduit orientation compared

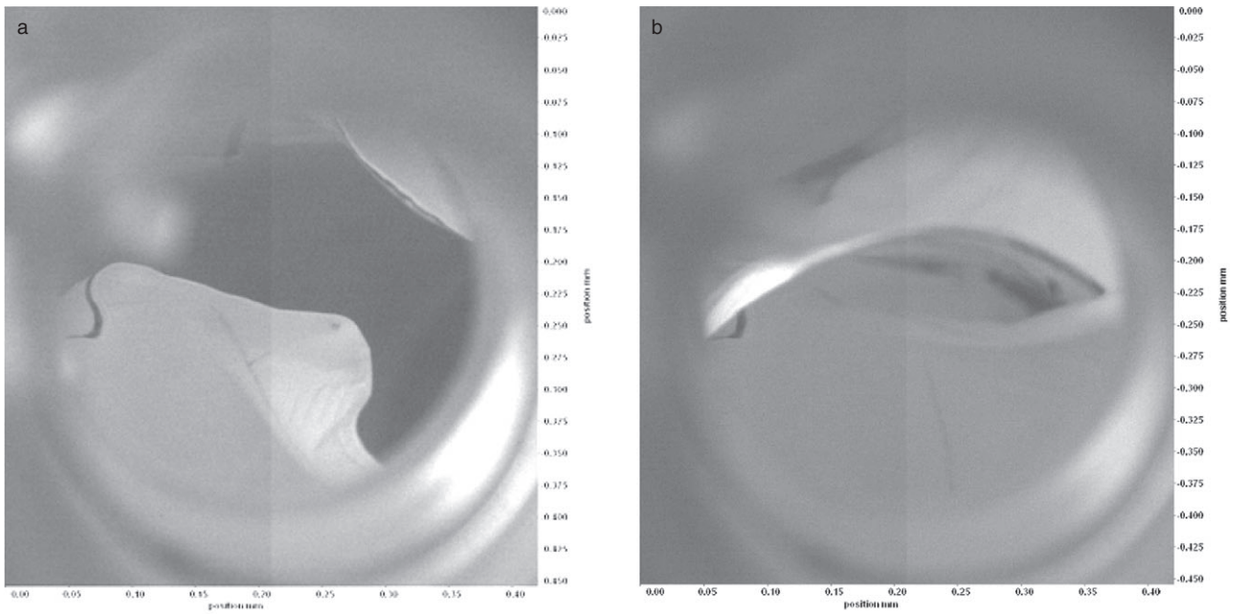

FIG. 5. Screen captures of C22 mm valve motion during systole (a) and diastole (b) phases indicated intact valve motion with asymmetrical valve motion.

TABLE 2. *Summary of valve performance parameters for the evaluation of valve location along the conduit curvature (R = 8.2 cm) for 16-mm diameter conduit (C16) tested under 1.5 L/min CO*

	Valve location					
	Proximal	Medial	Distal	Curvature	Straight	Anatomical
RF (%)	23 (2.1)	25 (2.2)	22 (1.8)	23 (2.1)	20 (2.0)	22 (1.7)
PPG (mm Hg)	11 (2.4)	14 (2.4)	14 (2.6)	13 (2.4)	*$P = 0.04$ 12 (2.4)	16 (2.7)
EAO (cm^2)	1.51 (0.1)	1.55 (0.1)	1.56 (0.1)	1.54 (0.1)	*$P = 0.09$ 1.47 (0.1)	1.48 (0.1)

* Errors spans given in parenthesis are calculated based on one standard deviation for 85% confidence interval and accounts for the cycle-to-cycle variations, transducer sensitivity, and repeatability error.

to the baseline horizontally oriented conduit ($P < 0.05$). These results indicate the competency of the bicuspid RVOT valve regardless of the conduit curvature or valve location along the conduit.

Three-dimensional conduit flow field

The CFD simulation demonstrated the flow skewness toward the major curvature of the conduit about 1 diameter distal from the inlet, based on the pulmonic conduit curvature. Hence, the flow velocity at the lesser curvature of conduit was slower than that at the major curvature during systole. Simulations indicated that lower curvature hosts the major backflow regime throughout late systole and diastole. Furthermore, flow profile was almost symmetrical along the curvature axis, which indicates balanced opening forces are exerted on each leaflet during the systole (Fig. 6). This result disagrees with the in vitro observations and may be caused by the blunt flow profile assumption imposed at the ventricle outlet.

DISCUSSION

The RV model demonstrated its utility by generating physiological flow and pressure waveforms. Transvulvar pressure measurements indicated significantly lower pressure drop, in turn lower flow impedance, for PTFE bicuspid valved conduits in comparison to the published mechanical valves tested in pulmonary position (12). However, it is important to note that the transvalvular pressure drop reported here indicates solely the hydraulic pressure drop due to viscous dissipation, as opposed to the pressure drop due to flow contraction at the valve outlet (i.e., vena contracta) measured by echocardiogram (19).

For a typical average diastolic pressure gradient ($\Delta P \sim 10$ mm Hg and systole-to-diastole ratio, $T_{sys/dys} \sim 0.7$), RF was estimated as a function of the operating CO, as shown in Fig. 7. The operating curves given for each conduit can be used as a new criterion for conduit selection, which will allow limitation of the RF under a desired threshold. For the conduits evaluated, the RF was limited under 20%, assuming full closure of valve under mean diastolic transvalvular pressure gradient of 10 mm Hg. We assumed that ΔP remains constant regardless of the change in operating CO. Future studies should investigate the actual relation between ΔP and CO for the cyanotic patient cohort in order to improve the accuracy of the proposed conduit selection method.

CFD simulations indicated lower flow in the lesser curvature of the conduit in the pulmonary position. These results agree with the author's clinical experience in the operating room as the lower leaflet of the previously designed tricuspid valved conduits were "stucked" due to insufficient forward momentum over the lower curvature (10).

The in vitro experiments demonstrated the competency of the bicuspid RVOT valve independent from the conduit curvature or valve location along the conduit. Current clinical understanding, which favors the distal valve placement with the hope of isolating the valve from the complex ventricle outflow, requires valve motion sensitivity analysis to the ventricle outflow profile. It may also be critical to determine if the valve location with respect to the

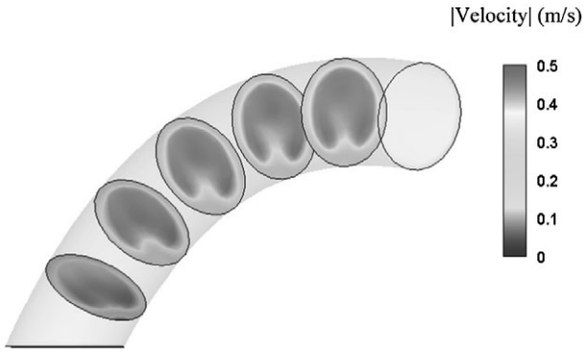

Fig. 6. Newtonian pulsatile blood simulated inside the 14 mm conduit for a CO of 1.2 LPM using second-order CFD solver. Time-averaged velocity contours shown during systole indicated lower velocity at the lesser curvature of the conduit.

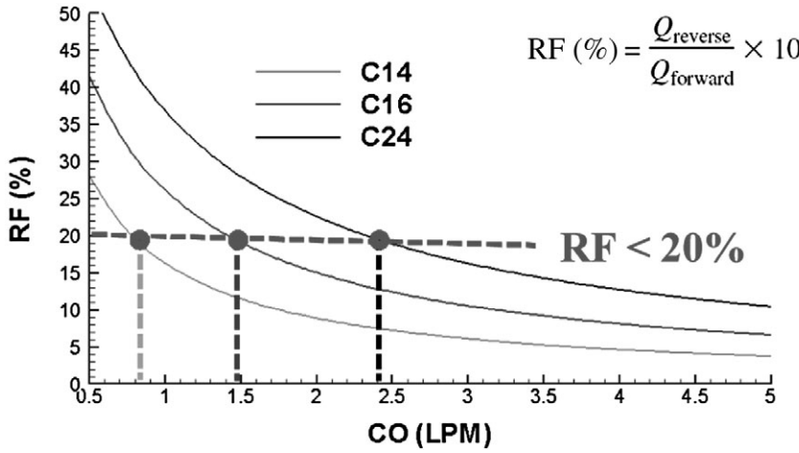

FIG. 7. Operating curves given for each conduit for estimating the RF based on constant diastolic pressure gradient (~10 mm Hg) and CO. This approach is proposed for conduit selection and allows limiting the RF under a desired threshold (<20%) as shown with the dashed line.

pulmonary bifurcation also affects the functional opening and closing of the valve, which should be addressed in the future. Improved numerical models incorporating the valve motion will help systematical analysis of each of the factors identified in this study and improve our understanding of valve behavior.

CONCLUSION

In vitro data with the bicuspid valved PTFE conduit coincides well with acceptable early clinical performance (mild insufficiency), with intact valve motion independent from the conduit curvature, orientation, or valve location, at the expense of increased diastolic flow regurgitation (25%). These findings document the baseline performance of the bicuspid valved conduit and will be used in future designs to improve valve competency.

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