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Patient-specific multiscale computational fluid dynamics assessment of embolization rates in the hybrid Norwood: effects of size and placement of the reverse Blalock–Taussig shunt¹

Ray Prather, John Seligson, Marcus Ni, Eduardo Divo, Alain Kassab, and William DeCampi

Abstract: The hybrid Norwood operation is performed to treat hypoplastic left heart syndrome. Distal arch obstruction may compromise flow to the brain. In a variant of this procedure, a synthetic graft (reverse Blalock–Taussig shunt) is placed between the pulmonary trunk and innominate artery to improve upper torso blood flow. Thrombi originating in the graft may embolize to the brain. In this study, we used computational fluid dynamics and particle tracking to investigate the patterns of particle embolization as a function of the anatomic position of the reverse Blalock–Taussig shunt. The degree of distal arch obstruction and position of particle origin influence embolization probabilities to the cerebral arteries. Cerebral embolization probabilities can be reduced by as much as 20% by optimizing graft position, for a given arch geometry, degree of distal arch obstruction, and particle origin. There is a tradeoff, however, between cerebral pulmonary and coronary embolization probabilities.

Key words: computational fluid dynamics, hypoplastic left heart syndrome, hybrid Norwood, lumped parameter model, patient specific, reverse Blalock–Taussig shunt, thrombus.

Résumé : La technique hybride de l'intervention de Norwood est utilisée pour traiter le syndrome d'hypoplasie du cœur gauche. L'obstruction de l'arc aortique distal peut compromettre le flux au cerveau. Dans une variante de cette intervention, on place un greffon synthétique (anastomose de Blalock–Taussig inversée) entre l'artère pulmonaire et le tronc artériel brachio-céphalique en vue d'améliorer le flux sanguin vers le haut du torse. Les thrombus provenant du greffon pourraient ainsi s'emboliser dans le cerveau. Dans ces travaux, nous avons étudié les schémas d'embolisation des particules en fonction de la position anatomique de l'anastomose de Blalock–Taussig inversée à l'aide de la mécanique des fluides numérique et du repérage des particules. Le degré d'occlusion de l'arc aortique distal et le lieu d'origine des particules influencent les probabilités d'embolisation dans les artères cérébrales. Il est possible de faire diminuer les probabilités d'embolisation cérébrale de jusqu'à 20 % en optimisant la position d'un greffon donné en fonction de la géométrie de l'arc en question, du degré d'occlusion distale de l'arc et de l'origine des particules. Il faut toutefois faire un compromis entre les probabilités d'embolisation cérébrale, pulmonaire et coronarienne. [Traduit par la Rédaction]

Mots-clés : mécanique des fluides numérique, syndrome d'hypoplasie du cœur gauche, Norwood hybride, modèle de paramètres concentrés, propre au patient, anastomose de Blalock–Taussig inversée, thrombus.

Introduction

Hypoplastic left heart syndrome (HLHS) is a congenital heart anomaly with an incidence of about 1 in 2000 live births. It is characterized by hypoplasia of the left ventricle, aortic arch hypoplasia, mitral atresia or stenosis, and aortic valve atresia or stenosis (Benjamin et al. 2017; Roger et al. 2012). Therapeutic options for HLHS are heart transplantation and strategies of staged reconstruction aimed at establishing a viable uni-ventricular circulation. The hybrid Norwood (HN) has emerged as a promising strategy for the first-stage reconstruction (Galantowicz et al. 2008; Bacha et al. 2006). HN avoids cardiopulmonary bypass and consists of branch pulmonary artery banding (Baker et al. 2013), stent-

ing of the ductus arteriosus, and balloon atrial septostomy, shifting the risk of major surgery to an older age with the expectation of improved survival as well as neurological outcome. The addition of a reverse Blalock–Taussig shunt (RBTS) sutured to the pulmonary trunk and anastomosed to the innominate artery aims to reinstate blood flow to the cerebral and coronaries arteries in cases of severe distal aortic arch stenosis (Caldarone et al. 2005, 2007) and as described on Nationwide Children's Hospital's website (<https://www.nationwidechildrens.org/>) (Nationwide Children's Hospital 2018). Our previous work aimed to understand the nature of the complex HN flow and to gauge the effectiveness of the RBTS to restore flow in cases of severe distal arch stenosis (Ceballos 2015;

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Fig. 1. Hybrid Norwood nominal fluid domain geometry (inlet, pulmonary trunk; LPA, left pulmonary artery; RPA, right pulmonary artery; RcorA, right coronary artery; LcorA, left coronary artery; LSA, left subclavian Artery; LCA, left carotid artery; RCA, right carotid artery; RSA, right subclavian artery; da, descending aorta). [Color online.]

Ceballos et al. 2012, 2015). This work is substantiated by similar results (Bove et al. 2008; Hsia et al. 2011). These studies demonstrated flow patterns such as recirculation zones, stagnation, and abnormal shear stresses. Combined with the fact that the RBTS is synthetic (usually consisting of polytetrafluoroethylene), these flow patterns put the RBTS at risk for thrombosis and thromboembolization. In this study, we conducted an analysis of thromboembolic probabilities for thrombi originating in various locations within the RBTS to establish the effect of shunt size and placement position on these rates (Seligson 2017). We specifically explored shunt sizes of 3, 3.5, and 4 mm. Our aim is to establish whether the RBTS size and placement can be tailored to reduce incidence of stroke due to shunt thromboembolism.

Materials and methods

Anatomic modelling

We constructed an anatomic model of the HN vasculature from a real patient's computed tomography scan using Mimics (Materialise, Leuven, Belgium), then added the RBTS using Solidworks (Dassault Systemes, Waltham, Massachusetts, USA) (Fig. 1). We meshed the resulting anatomic model, then calculated the flow through the domain using computational fluid dynamics (CFD) using StarCCM+ (CDAdapco-Siemens, Plano, Texas, USA).

Flow calculations

To calculate the flow field, StarCCM+ employs a finite volume approach to solve the continuity and momentum equations (eqs. 1 and 2). A second-order temporal discretization has been used to retain accuracy in computing the discretized transient terms. Convective terms are resolved with a second-order scheme as well.

$$(1) \quad \nabla \cdot \vec{V} = 0$$

$$(2) \quad \rho \frac{\partial \vec{V}}{\partial t} + \rho(\vec{V} \cdot \nabla) \vec{V} = -\nabla p + \mu \nabla^2 \vec{V}$$

A segregated flow solver is implemented to solve the 3-dimensional flow field. Both velocity and pressure are under-

Fig. 2. Computational fluid dynamics (CFD) – lumped parameter model (LPM) coupling scheme guided by a Java macro regulating the data exchange between the CFD code and the LPM circuit. BC, boundary conditions; RK, Runge-Kutta solver; Rs, flow resistances. [Color online.]

relaxed to maintain a stable solution. Blood was modeled as a non-Newtonian incompressible fluid with a density of $\rho = 1060 \text{ kg/m}^3$ and dynamic viscosity, $\mu(\dot{\gamma})$, using a 3-parameter modified Carreau-Yasuda model (eq. 3).

$$(3) \quad \mu(\dot{\gamma}) = \mu_{\infty} + (\mu_0 - \mu_{\infty}) \frac{1}{[1 + (\lambda \dot{\gamma})^2]^{\frac{1}{3}}}$$

Here, $\dot{\gamma}$ is the shear rate and the model constants are the viscosity at high shear rate μ_{∞} , the viscosity at zero shear rate μ_0 , and relaxation time λ depend on blood hematocrit (Long et al. 2005; Good et al. 2016). We used values corresponding to a 40% hematocrit: $\mu_{\infty} = 4 \text{ cP}$, $\mu_0 = 8 \text{ cP}$, and $\lambda = 0.313 \text{ s}$.

Boundary conditions are provided by a lumped parameter model (LPM) circuit that is coupled to the CFD (Figs. 2 and 3). The LPM circuit is as outlined in previous work carried out by our group (Prather 2015; Prather et al. 2017) and substantiated by similar approaches. The LPM provides 1-dimensional inlet mass flow rates and stagnation pressure to the fluid domain while the CFD returns surface averaged pressure and mass flow rates at locations corresponding to the circuit nodes back to the LPM along with initial conditions. The LPM model described by Ceballos (2015) and Ceballos et al. (2012) based on the work carried out by Faragallah et al. (2012) was modified to reflect a more physiologically correct flow split at the coronaries. Sankaran et al. (2012) observed a 70%–30% split between the left and right coronary arteries. To achieve this, the arterial coronary resistances were manipulated to either enhance (left) or reduce (right) flow while retaining the appropriate overall coronary flow to cardiac output ratio. Figure 3 displays the full LPM circuit.

Following initial tuning of the LPM model, the LPM–CFD coupling is used to iteratively adjust the boundary conditions to attain consistent and physiologically correct flow field. Once pressure and mass flow rates variations fall below threshold values, the flow field is deemed converged. The flow field is in turn used to track particles in the Lagrangian frame as described in the sequel.

For each configuration, a structured mesh is generated, including a 7-cell thick prism layer, which extrudes from the domain wall (Fig. 4). Volumetric refinement at the pulmonary bands as well as curvature refinement was carried out due to the sharp

Fig. 3. Full lumped parameter model circuit used for all configurations. [Color online.]

Fig. 4. Sample full domain mesh (left) and prism layer mesh in pulmonary artery (right). [Colour online.] **Table 1.** Mesh data for all reported geometries.

Stenosis level	Shunt size and placement	Cell count
0%	3 mm, nominal	2 012 153
	3.5 mm, nominal	2 022 188
	4 mm, nominal	2 045 489
90%	3 mm, nominal	2 325 633
	3.5 mm, nominal	2 342 107
	4 mm, nominal	2 271 028
0%	3.5 mm, option 1	612 585
	3.5 mm, option 2	616 846
	3.5 mm, option 3	579 635

lumen area reduction to retain computational accuracy. Table 1 summarizes the data relative to cell count for each model analyzed. A grid independence study not reported here was carried out for the new configurations.

Given the Eulerian–Lagrangian coupling and the mesh count, this problem was parallelized on a local cluster where the domain was portioned on an average of 16 CPUs per simulation. A total of 3 heart cycles per simulation for a total physical time of 1.5 s (0.5 s per heart cycle) are simulated.

Particle tracking

Particle motions were calculated in the Lagrangian frame (eq. 4). We accounted for blood-to-particle and particle-to-wall interactions while neglecting particle-to-particle interaction. Forces on the particles included gravity, drag, Saffman lift and added mass (eqs. 5 and 6).

$$(4) \quad m_p \frac{d\vec{V}_p}{dt} = \vec{F}_{\text{body}} + \vec{F}_{\text{surface}}$$

$$(5) \quad \sum \vec{F}_{\text{body}} = \vec{F}_{\text{gravity}}$$

$$(6) \quad \sum \vec{F}_{\text{surface}} = \vec{F}_{\text{drag}} + \vec{F}_{\text{added mass}} + \vec{F}_{\text{Saffman}}$$

The added mass accounts for the inertia of the surrounding volume of fluid displaced by the particles as they accelerate or decelerate in the flow, while the Saffman lift is a shear lift force perpendicular to the flow direction that originates from inertia effects in the viscous flow around the particle. We modelled thrombi (particles) as solid spheres of set density $\rho = 1116.73 \text{ kg/m}^3$

Fig. 5. Particle release grids along shunt (injection_grid 1, proximal; injection_grid 2, medial; injection_grid 3, distal). [Color online.]

and varying size between 1 mm and 2 mm in diameter. We investigated 3 separate particle origins, or “release locations” — at the proximal, or pulmonary trunk end, at the distal, or innominate artery end, and midway between these within the graft (Fig. 5). We introduced particles in the fluid domain by means of injector grids (Fig. 5) that release particles randomly in time and in space over the injector cross-section grids. Particles are assumed to have zero initial velocity.

The particle release rate per injector is prescribed by a time-based table that has a portion of the points in the grid release a particle at random time-steps throughout the run. The number of selected grid points per injector releasing a particle at a time-step is determined by a fixed value, namely the point inclusion probability. The particle time-table ensures temporal randomness while StarCCM+ allows randomization of spatial release at every time-step. Particle interactions are limited to particle–fluid and particle–wall, the latter regulated by restitution coefficients for perfectly elastic collisions. Particles are tracked in the anatomic

Fig. 6. Proposed shunt positioning to investigate embolization rate optimization: (a) increased distal anastomosis angle of implantation, (b) rotated shunt out of plane with a shallow anastomosis angle, and (c) shortened shunt anastomosis located proximal to the aortic and pulmonary trunk roots. [Color online.]

domain and boundary counters at the outlets allow evaluation of particle transport statistics.

We investigated models with 0% and 90% distal aortic arch stenosis, and 3 mm, 3.5 mm, and 4 mm diameter RBTS grafts for each degree of arch stenosis. Based on previous studies conducted by our group (Ceballos 2015; Ceballos et al. 2012, 2015) that determined that a 3.5 mm shunt ensures enhanced cerebral vessel and coronary perfusion, 3 alternate orientation options of the RBTS with 3.5 mm diameter with 0% aortic arch stenosis case were generated. The alternate geometries vary in anastomosis location and angle as follows: (i) increased distal anastomosis angle of

implantation (Fig. 6a); (ii) rotated shunt out of plane with a shallow anastomosis angle (Fig. 6b); and (iii) shortened shunt anastomosis located proximal to the aortic and pulmonary trunk roots (Fig. 6c). The nominal RBTS graft implantation (Fig. 4) is at 90° to the innominate. Starting from the nominal graft placement, we moved to (i) increase angle of anastomosis at the innominate artery by 36° while keeping the graft on the same graft centerline plane, (ii) rotate the shunt out of plane by 70° aligning the outlet centerline with the centerline of the distal aortic arch, and (iii) translate the distal anastomosis 17 mm from the innominate artery takeoff caudally along the ascending aorta towards the coronary arteries.

Results

Particle data were collected for all nominal geometries and the optional models. Figures 7–10 display sample particle tracks for the 3.5 mm shunt size, 0% distal arch stenosis, and for 1 mm particle size. Similar representations were obtained for all graft diameters. Each column contains a sequence of images for a single heart cycle for particles released at the proximal, medial, and distal grid in the graft with an adjacent heart cycle plot to display the sampling instant. Comparable displays for particle tracks for other diameters may be found in the supplementary material accompanying this manuscript².

For particle release from the proximal grid, the effect of diastolic back flow in the shunt can be clearly seen for all graft and particle sizes studied. Particles are transported from the shunt to the pulmonary trunk. Shortly thereafter, however, the heart cycle enters the systolic phase and strong ventricular ejection pushes particles towards the ductus arteriosus. This pattern presents 2 main potential outcomes as particles move towards the descending aorta: they may embolize to the pulmonary arteries (corresponding to the clinical scenario of pulmonary thromboembolism) or they proceed to the descending aorta and may embolize downstream in the lower body circulation. With increasing graft diameters, the portion of the shunt lumen experiencing back flow decreases, allowing for more particles to travel towards the distal portion of the graft. In systole, this results in a much larger number of particles being pushed into the aortic arch and in particular into the right cerebral vessels. Larger particles carry more momentum, which may result in deviation from flow streamlines especially near distal shunt anastomosis and vessel bifurcations.

Particles originating from the midline grid experience graft back flow as well for all graft and particle sizes. Because of their initial position, however, these particles infrequently reach the pulmonary trunk. In fact, they tend to behave as particles originating from the proximal grid, both remaining within the graft lumen for a greater fraction of the cardiac cycle. Particles that do travel upstream enter the aortic arch and right cerebral vessels and, presumably, to the brain. Additionally, with larger graft diameter and (or) larger particle size, fewer particles experience retrograde flow in diastole.

The most evident feature of particles released from the distal grid is an increased probability of transport to the aortic arch and branching vessels. This is true for all graft and particles sizes studied. The clinical consequence potentially would be cerebral or coronary embolism. In particular, particles released in the aortic arch and experiencing larger residence time in the arch (especially in diastole) have a greater probability of embolization to the coronary arteries (Fig. 7). If any particle happens to be caught in back flow during diastole, they may behave as particles originating from the midline of the graft, but for the most part, in systole they will be transported antegrade and out of the graft. The few

²Supplementary data are available with the article through the journal Web site at <http://nrcresearchpress.com/doi/suppl/10.1139/cjpp-2018-0002>.

Fig. 7. Coronary streamlines combined with 1 mm particles. [Color online.]

particles that do travel retrograde out of the graft may ultimately reach the descending aorta by way of the ductus arteriosus.

Overall, examination of the flow patterns illustrates the “double jeopardy” of clot formation in the RBTS — particles traveling antegrade and beyond the distal end of the graft will embolize to either the coronary arteries or arch vessels (including cerebral vessels), potentially resulting in myocardial injury or stroke. Particles traveling retrograde and beyond the proximal end of the graft will embolize either to the descending aorta or pulmonary arteries, resulting potentially in either abdominal organ embolization or pulmonary embolism. A rigorous patient-specific optimization scheme would optimize RBTS position to minimize particle embolization to the cerebral and coronary arteries, with the hope that embolization to the lung or descending aorta will be less clinically consequential.

Overall, the 0% stenosis case involves higher embolization rates (Fig. 11, top). For the 0% stenosis case, RBTS graft diameter did not significantly impact the percentage of total embolic events with 55.92% for 3 mm graft, 54.34% for a 3.5 mm graft and 54.22% for a 4 mm graft. Focusing on pulmonary embolism, the 3 mm graft displayed lower probabilities than the larger grafts. In general, the 3 mm graft resulted in lower probability of coronary embolization, followed by the 3.5 mm graft. Qualitatively there seemed to be an inverse relationship between cerebral and coronary arterial particle embolization probability.

The 90% stenosis case showed lower overall embolization probability than that in the 0% stenosis case (Fig. 11, bottom). In this case, graft diameter was an important factor, with embolization probabilities of 33.95% for a 3 mm shunt, 44.61% for a 3.5 mm shunt, and 49.01% for a 4 mm shunt. On the other hand, pulmonary embolism does not appear strongly correlated to graft diameter. Coronary embolization probability was directly related to increasing shunt diameter. In general, there was a direct relationship between cerebral and coronary embolization probabilities.

As shown in Fig. 11, graft diameter clearly plays a role in potentially reducing thromboembolic events. The sharp reduction of more than 10% observed with a 3 mm shunt 90% distal arch stenosis proves that surgical techniques can be optimized in this case to reduce stroke even though in the absence of distal arch stenosis, shunt size does not significantly impact thromboembolic rates. A near 2% reduction in coronary embolization probability with the 3 mm graft also supports the notion that graft diameter is a factor in embolization probabilities. Regarding the probability of pulmonary embolization, for the 0% stenosis case, there was no significant dependence of embolization probability on graft diameter. For the 90% stenosis case, the 3.5 mm and 4 mm grafts are associated with reduced pulmonary embolization probabilities, as compared with those of the 3.0 mm graft.

To further investigate the graft positional factors that may influence embolization probabilities to the right cerebral vessels, we varied distal anastomosis angle and proximal and distal anastomosis locations on their respective vessels. Starting from the nominal graft placement, we moved to increase angle of anastomosis at the innominate artery by 36° while keeping the graft on the same graft centerline plane (option 1), rotate the shunt out of plane by 70° to have an outlet normal in line with the aortic arch (option 2), and translate the distal anastomosis 17 mm from the innominate artery takeoff caudally along the ascending aorta towards the coronary arteries (option 3). We held the graft diameter constant at 3.5 mm between the 3 options in Fig. 6 based on previous studies (Ceballos et al. 2015; Ceballos 2015) that examined 3.0, 3.5, and 4 mm RBTS shunt diameters and found that the 3.5 mm graft provided the best option from the point of view of restoring coronary blood flow in the presence of distal arch stenosis while providing the most favorable hemodynamics when implanted prophylactically.

Overall, option 3 shows the lowest cumulative thromboembolic probability with 52.70%, while option 2 has 59.30% and option 1

Fig. 8. Nominal 3.5 mm reverse Blalock–Taussig shunt 0% stenosis 1 mm proximal particle release. [Color online.]

Fig. 9. Nominal 3.5 mm reverse Blalock–Taussig shunt 0% stenosis 1 mm medial particle release. [Color online.]

Fig. 10. Nominal 3.5 mm reverse Blalock–Taussig shunt 0% stenosis 1 mm distal particle release. [Color online.]

Fig. 11. Embolization rates for the patient-specific model with 0% stenosis (top) and 90% distal arch stenosis (bottom). BT, Blalock–Taussig. [Color online.]

Fig. 12. Embolization rates for the 0% distal arch stenosis 3.5 mm shunt patient-specific model for the 3 different options. [Color online.]

has 63.23% (Fig. 12). Option 3 leads to the lowest stroke risk being nearly half that of options 1 and 2. Option 3, however, displays a pulmonary embolism risk more than 3 times higher compared with the other 2 options. Option 1 is most favorable in this case. This sharp distinction is entirely due to the graft placement and length. As the graft length is much less than that in the nominal case, throughout a heart cycle, a larger amount of particles enter the pulmonary trunk; therefore, having a high probability of embolizing to the pulmonaries. Option 1 results in the lowest rate of myocardial infarction among the 3 configurations, while options 2 and 3 present more than twice that amount. In option 3, larger coronary embolization rates are due to the distal shunt anastomosis proximity to the aortic root. Option 2 leads to particles released in the aortic arch to experience large residence time in the volume between the innominate take-off and the coronar-

ies causing them to ultimately be transported to the coronaries. For the 3 options, stroke risk and pulmonary embolism risk appear to be inversely correlated.

When comparing the nominal case for a 3.5 mm graft with 0% stenosis with the new configurations thromboembolic incidence can be reduced from 54.34% to 52.70% (option 3). However, incidence may also be increased from 54.34% to 63.23% (option 1). Upon closer inspection, beneficial effect becomes more evident. Option 3 shows more than a 2-fold decrease in embolization probability from 47.68% to 22.41%. Option 2 displays as much as a 7% decrease in embolization probability. Option 1 shows an increase in cerebral embolization probability but a noticeable reduction in pulmonary embolization probability from 5.59% to 3.98%. Pulmonary embolism incidence for options 2 and 3 increases up to 3 times the nominal amount. Coronary embolization probabilities consistently increase across all option configurations by as much as 13 times (option 2) from 1.07% up to 13.22%. These new configurations target the reduction of stroke risk by redirecting thrombi travelling out of the shunt away from the cerebral vessels. Particles transported into the aortic arch (aimed away from the cerebral vessels) either flow towards the distal portion of the aortic arch or flow towards the aortic root, causing higher coronary embolization rates.

Stroke risk can be reduced by modifying the graft anastomosis configuration. However, there is a clear tradeoff between reducing stroke incidence and increased myocardial infarction and pulmonary embolisms. Within the limited exploration in this study, option 3 may be the best tradeoff. While halving stroke probability (from 47.68% to 22.41%), coronary embolization is 10-fold larger (from 1.07% to 11.82%) and pulmonary embolism grow 3-fold (from 5.59% to 18.47%). Additional variance may be introduced on a case-by-case basis for different patient-specific geometries.

Discussion

The HN procedure is performed as a first stage palliation of HLHS. A complication of the HN is distal arch obstruction, which compromises flow to the coronaries and upper systemic circulation. As a countermeasure, a synthetic graft, the RBTS, is introduced between the pulmonary trunk and the innominate artery to enhance flow to the aortic arch. Previous studies have compared the hemodynamics of the HN and standard Norwood repair (Hsia et al. 2011), explored the effects of pulmonary banding in the HN (Baker et al. 2013), explored the ability of the RBTS to restore coronary blood flow in the presence of various degrees of distal arch stenosis (Ceballos et al. 2012), and explored shunt flow with and without distal arch obstruction suggesting that a 3.5 mm diameter graft provides the best compromise shunt size when the RBTS is implemented prophylactically (Ceballos et al. 2015; Ceballos 2015). Moreover, the latter computational hemodynamic studies have also suggested that the RBTS graft has the potential to develop pathological flows that may be thrombogenic. Thrombi originating in the shunt risk embolization to the brain. In this study, we analyze the correlation between shunt size and placement to embolization probabilities. Furthermore, we target the reduction of stroke rates by modifying the graft configuration to redirect particles away from the cerebral circulation. The aim is to identify factors influencing embolization rates. The multiscale CFD model utilized in this study implemented a non-Newtonian blood model, a patient-specific geometry, and pulsatile flow conditions. The CFD fluid domain was coupled to a LPM and iterated to ensure a converged boundary condition before introducing the Lagrangian phase tracking model for transport of thrombi.

Our multi-scale patient-specific HN model predicts that for nominal RBTS implantation, shunt size has little influence on thromboembolic incidence when no stenosis is present. Stroke probability decreases 15%–20% when distal arch obstruction is present. Moreover, for a severe 90% distal arch stenosis, stroke

rates are sensitive to shunt size. Closer inspection reveals that graft size can have beneficial influence on stroke probability in this case, and more than 10% reduction can be achieved by utilizing a smaller shunt size of 3 mm for severe distal arch obstruction. The rates of pulmonary and coronary embolism are not significantly different with variation of shunt size; however, these rates are higher with 90% stenosis as compared with no stenosis. Pulmonary embolism rates double while coronary embolism quadruple in the presence of severe stenosis. Consequently, in the presence of distal arch stenosis, our current results suggest that a 3 mm RBTS could be considered as advantageous in reducing cerebral and coronary thromboembolic events while offering no significant improvement in pulmonary embolization rates.

In case of prophylactic implementation of the RBTS in the absence of distal arch stenosis, we explored whether improvement in thromboembolism rates can be achieved by optimally tailoring the shunt implantation. Here, we focus on the 3.5 mm RBTS as suggested by (Ceballos et al. 2015; Ceballos 2015) and we investigated several discrete shunt placements and orientations. In option 1, steepening the distal arch anastomosis angle relative to the nominal implantation in an attempt to redirect the thrombus away from cerebral vessels (Fig. 6) had adverse effects of increasing stroke probability by 6% and coronary embolization by 5% but a positive effect of reducing pulmonary embolism rates by 2%, leading to a combined embolism rate (63.23%) that was higher than nominal (54.34%). In option 2, rotating the graft out of plane reduced stroke probability by 7%, but augmented coronary embolism probability by 13% leading to a combined embolism rate (59.3%) that was also higher than nominal (54.34%). However, in option 3, translating the graft closer to the aortic root reduced stroke probability by 25%, although pulmonary embolism doubled and coronary embolism probability grew 10-fold relative to the nominal case resulting in a reduced combined embolism rate (52.7%) relative the nominal (54.34%). In the absence of arch stenosis, manipulation of the 3.5 mm graft implantation lead to significant improvement in stroke risk that was accompanied by acute increases in other thromboembolic events. Our results suggest that optimizing RBTS placement in the absence of arch stenosis from the perspective of reducing thromboembolisms involves competing factors and may require careful trade-off in optimization on a patient-specific basis.

Our study was limited to a single-patient geometry. Beneficial modifications to the RBTS implantation found in this study may not yield a similar outcome for other patients. Future work should consider a larger number of patient-specific geometries. Limitations of the model used in this study include rigid vessel walls. Future studies may consider compliant vessels by generating wall thickness and using a suitable arterial mechanical model in a fluid-structure interaction multiscale hemodynamics model. However, such calculations are highly computationally intensive and may not be suitable for clinical applications. Another limitation in the current work, is that the thrombi are modeled as point particles in a Lagrangian phase with elastic particle-to-wall interactions. Future work could consider introducing particle-to-particle interactions and partially elastic collisions. Moreover, more complex discrete element model or a dynamic fluid-body interaction model may be used to simulate particles with discrete dimensions interacting with each other and the walls accounting for damping and potential deformation. Such options also significantly add to the computational burden of the simulation.

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