Cannulation Strategy for Aortic Arch Reconstruction Using Deep Hypothermic Circulatory Arrest

Diane de Zélicourt, PhD, Philsub Jung, BA, Marc Horner, PhD, Kerem Pekkan, PhD, Kirk R. Kanter, MD, and Ajit P. Yoganathan, PhD

Wallace H. Coulter Department of Biomedical Engineering, Georgia Institute of Technology, Atlanta, Georgia; ANSYS Inc, Evanston, Illinois; College of Engineering at Carnegie Mellon University, Pittsburgh, Pennsylvania; and Division of Cardiothoracic Surgery, Emory University, Atlanta, Georgia

Background. **Aortic arch reconstruction in neonates is commonly performed using deep hypothermic circulatory arrest. However, concerns have arisen regarding potential adverse neurologic outcomes from this complex procedure, raising questions about the best arterial cannulation approach for cerebral perfusion and effective systemic hypothermia. In this study, we use computational fluid dynamics to investigate the effect of different cannulation strategies in neonates.**

Methods. **We used a realistic template of a hypoplastic neonatal aorta as the base geometry to investigate four cannulation options: (1) right innominate artery, (2) innominate root, (3) patent ductus arteriosus (PDA), or (4) innominate root and PDA. Performance was evaluated according to the numerically predicted cerebral and systemic flow distributions compared with physiologic perfusion under neonatal conditions.**

Results. **The four cannulation strategies were associated with different local hemodynamics; however, this did not translate into any significant effect on the measured flow distributions. The largest difference only represented 0.8% of the cardiac output and was measured in the innominate artery, which received 23.2% of the cardiac output in option 3 vs 24% in option 4. Pulmonary artery snaring benefited all systemic vessels uniformly.**

Conclusions. **Because of the very high vascular resistances in neonates, downstream vascular resistances dictated flow distribution to the different vascular beds rather than the cannulation strategy, allowing the surgical team to choose their method of preference. However, patients with aortic coarctation warrant further investigation and will most likely benefit from a 2-cannulae approach (option 4).**

(Ann Thorac Surg 2012;94:614–21)

The use of deep hypothermic cardiac arrest (DHCA) has been established as a standard procedure for neonates born with a hypoplastic left heart syndrome who require surgical repair of their hypoplastic aortic arch. Unfortunately, DHCA has also been associated with significant complications, including impaired neurodevelopment [1], and non-neurologic morbidities such as pulmonary and renal dysfunction [2] and multiorgan failure. Although the complications associated with DHCA are no doubt multifactorial, proper perfusion of all vascular beds during the cooling process is a primary requirement, ensuring that not only the brain but also all peripheral organs are sufficiently hypothermic.

Hypoplastic aortic arches represent nonstandard and complex surgical anatomies that lend themselves to several possibilities for arterial cannulation, including insertion into the (1) innominate artery [3], (2) right subclavian artery [4], or (3) patent ductus arteriosus (PDA) [5]. The pulmonary arteries (PAs) or the PDA are also commonly snared in an effort to further increase systemic blood flow. However, the exact effect of the different options on the actual cerebral perfusion in HLHS patients remains unknown. Likewise, whether PA or PDA snaring truly brings a benefit in cerebral perfusion remains to be demonstrated.

Experimental and computational bioengineering studies have begun to address these issues, investigating the effect of cannula design [6] and location [7] on perfusion characteristics in normal aortic arches. The recent study of Kauffman and colleagues [7], for example, compares the hemodynamic characteristics of a standard bypass configuration with different cannula insertion points and angles for a healthy aortic arch configuration. Yet, the geometry of hypoplastic aortic arches and associated hemodynamics [8] drastically differ from that of normal aortic arch configuration and are highly variable from patient to patient. In addition, the neonatal circulation is characterized by a significantly lower cardiac output and very high vascular resistances compared with adults. These challenges limit the generalization of former stud-

Accepted for publication March 21, 2012.

Address correspondence to Dr Yoganathan, Wallace H. Coulter School of Biomedical Engineering, Georgia Institute of Technology and Emory University, 313 Ferst Dr, Atlanta, GA 30332-0535; e-mail: ajit.yoganathan@bme.gatech.edu.

Published by Elsevier Inc

0003-4975/$36.00
http://dx.doi.org/10.1016/j.athoracsur.2012.03.053

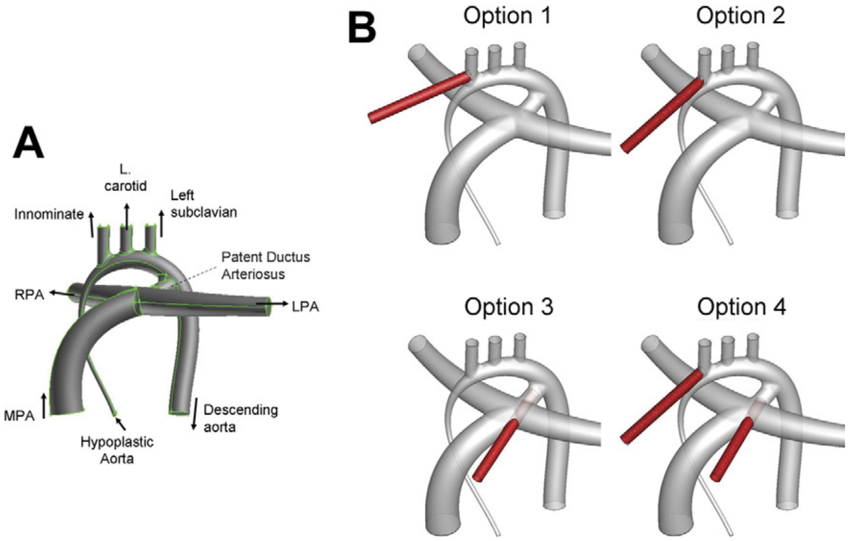

Fig 1. (A) Geometry of the idealized hypoplastic aorta. (B) The cannula insertion locations are shown for the four options. The cannula is shown in red, and the hypoplastic aorta is shown in gray. (L carotid = left carotid; LPA = left pulmonary artery; MPA = main pulmonary artery; RPA = right pulmonary artery.)

ies performed on normal adult aortas to patients with congenital HLHS.

The lack of bioengineering studies on neonatal arches may be partly explained by the difficulty to access in vivo anatomies and precise flow information. Indeed, exposure to radiation for computed tomography is not desirable at such a young age, and sedation is required for magnetic resonance imaging. Likewise, transcranial and intraoperative pulsed-Doppler ultrasound measurements lead to large measurement errors due to the unclear probe orientation on tiny great vessels. However, to achieve a comparative assessment on the effect of cannulation strategies on hemodynamics, the inclusion of all patient-specific details may not yet be necessary, and significant insights may still be gained through a realistic idealized hypoplastic aortic arch template. We therefore developed a computational test-bed to isolate the effect of different cannulation locations and PA snaring on the flow distribution of a neonatal hypoplastic aortic arch during systemic cooling. This study builds on our previous work [8, 9], a bioengineering study that investigated the hemodynamics of hypoplastic and congenitally defective aortas.

Material and Methods

Cannula Insertion Locations

The baseline aortic arch anatomy, inclusive of the PDA, corresponds to the realistically idealized hypoplastic aortic arch template reconstructed by Pekkan and colleagues [8] (Fig 1, top panel), based on the vessel dimensions reported by 3 pediatric cardiologists and an extensive literature search (eg, Ilbawi and colleagues [10]). Four common cannula insertion locations (with cannula tips of 4 mm in diameter) were incorporated into this geometry (Fig 1).

- Option 1 illustrates a cannula inserted into the innominate artery. Because cannula insertions into or around the innominate artery may be expected to strongly favor flow to that vessel, the cannula in option 1 was inserted into the proximal section of the vessel to determine the lower bound of the expected innominate flow rate.
- Option 2 presents a variation of that design, with the cannula inserted into the root of the innominate artery and oriented toward the branching between the aortic arch and the left carotid artery.
- Option 3 illustrates a cannula that is inserted through the PDA.
- Option 4 models a bifurcated cannula with 2 tips, 1 inserted into the innominate root and 1 through the PDA, thereby combining the configurations in options 2 and 3.

Computational Fluid Dynamic Simulations

The computational method used in this study has been validated against in vitro experiments [11] and in vivo piglet pressure data during bypass [8]. Briefly, all geometries were meshed in GAMBIT (ANSYS Inc, Canonsburg, PA), using the HexCore/TGrid scheme. A nonuniform mesh resolution was used to properly capture the regions of high velocity while minimizing the computational cost. A preliminary mesh refinement investigation indicated that the pressure and flow distributions were grid-insensitive when using a grid spacing of 0.15 mm or less in the high-velocity regions. Accordingly, a spacing of 0.15 mm was applied to the regions of high velocity, and a spacing of 0.3 or 0.6 mm was used in the regions of lower velocity, such as the PAs or ascending aorta, resulting in approximately 1 million elements for each configuration. The flow simulations were conducted in FLUENT (ANSYS Inc), using an unsteady, second-order, implicit formulation [8, 11]. The convergence criterion was set to 10^{-5} for all degrees of freedom.

The simulation set-up and boundary conditions are summarized in Figure 2. Because cardiopulmonary bypass delivers a nonpulsatile flow rate, neglecting aortic wall motion is considered a fair assumption, and the

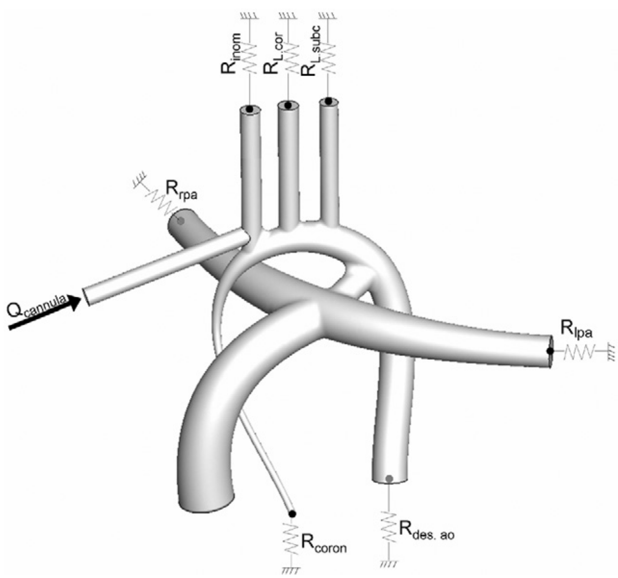

Fig 2. Schematic representation shows the inflow and outflow boundary conditions. (coron = coronary; des ao = descending aorta; inom = inominate; L cor = left coronary; L subc = left subclavian; lpa = left pulmonary artery; Q = flow rate; R = resistance; rpa = right pulmonary artery.)

vessel walls were modeled as rigid no-slip boundaries. Resistance boundary conditions were imposed at the outlets to represent the downstream systemic vasculature. The resistance values were calculated by conducting a set of preliminary simulations without any cannula until the computed mass flow rate at each outlet matched physiologic flow distributions for neonates. In these preliminary simulations, blood flow rate was set to 0.87 L/min, representing the cardiac output for a neonate weighing 3.5 kg [12]. The target physiologic neonatal flow distributions were determined assuming an equal distribution to the superior and inferior systemic beds, and that before closure of the PDA, about 30% of the flow went to the PAs. Retrograde perfusion of the coronary arteries (4% to 5% of the cardiac output) was modeled by setting an outflow resistance boundary condition at the hypoplastic ascending aorta cross-section. Matching the desired mass flow splits constrains the pressure gradients across the aorta but leaves one degree of freedom for the absolute pressure values. The resistances were thus adjusted for a mean aortic pressure of 50 mm Hg.

The vascular resistances defined in the preliminary simulations were assumed to hold constant during perfusion. The perfusion flow rate was set to 0.525 L/min, as is customary during DHCA. For option 4, with a dual cannula, the inflow rate was divided equally between the 2 cannulae. PA snaring was modeled by blocking the pulmonary outlets (modeled as wall boundary conditions) while maintaining the systemic resistances constant. PDA snaring was not explicitly modeled because it was expected to yield flow distributions similar to those with PA snaring given that both methods exclude flow from the PAs.

Results

Vascular Resistances

The neonatal resistances are 7,000, 2,370, 5,923, 3,933, 1,189, and 2,740 MPa.s.m^{-3} for the coronaries, innominate artery, left carotid, left subclavian, descending aorta, and pulmonary arteries, respectively. This corresponds to global superior and inferior systemic vascular resistances of 148 and 149 Woods units, respectively. These values fall within a range close to those reported by Lagana and colleagues [13] in their model of a neonatal Norwood circulation.

Effect of Cannulation Location on Flow Distribution (PAs Snared)

Simulation results for DHCA with the PAs snared are summarized for blood flow distribution in Table 1. Flow distributions measured in the neonatal hypoplastic aorta (without any cannula), with and without PA snaring, are provided as reference. The corresponding flow pathways are illustrated in Figure 3 using three-dimensional streamlines color-coded by velocity.

Table 1. Flow Distributions Measured in the Control Cases and Four Cannulation Options With Pulmonary Artery Snaring During Deep Hypothermic Circulatory Arrest[a]

Test Case	Innominate	Left Carotid	Left Subclavian	Cor	Descending Aorta	PA Left	PA Right
Controls							
Hypoplastic aorta	16.4	6.6	9.9	4.7	33.2	14.6	14.6
Hypoplastic aorta with PA snared	23.2	9.3	14.1	6.6	46.8	0.0	0.0
Cannula options with PA snaring							
Option 1	24.0	9.1	14.0	6.4	46.5	0.0	0.0
Option 2	24.0	9.4	14.0	6.3	46.3	0.0	0.0
Option 3	23.2	9.3	14.1	6.5	46.9	0.0	0.0
Option 4	23.5	9.4	14.1	6.4	46.6	0.0	0.0

[a] Flow distributions are calculated as percentage of the perfusion flow rate with a perfusion flow rate of 0.525 L/min.

Cor = retrograde flow to the coronary arteries; PA = pulmonary artery.

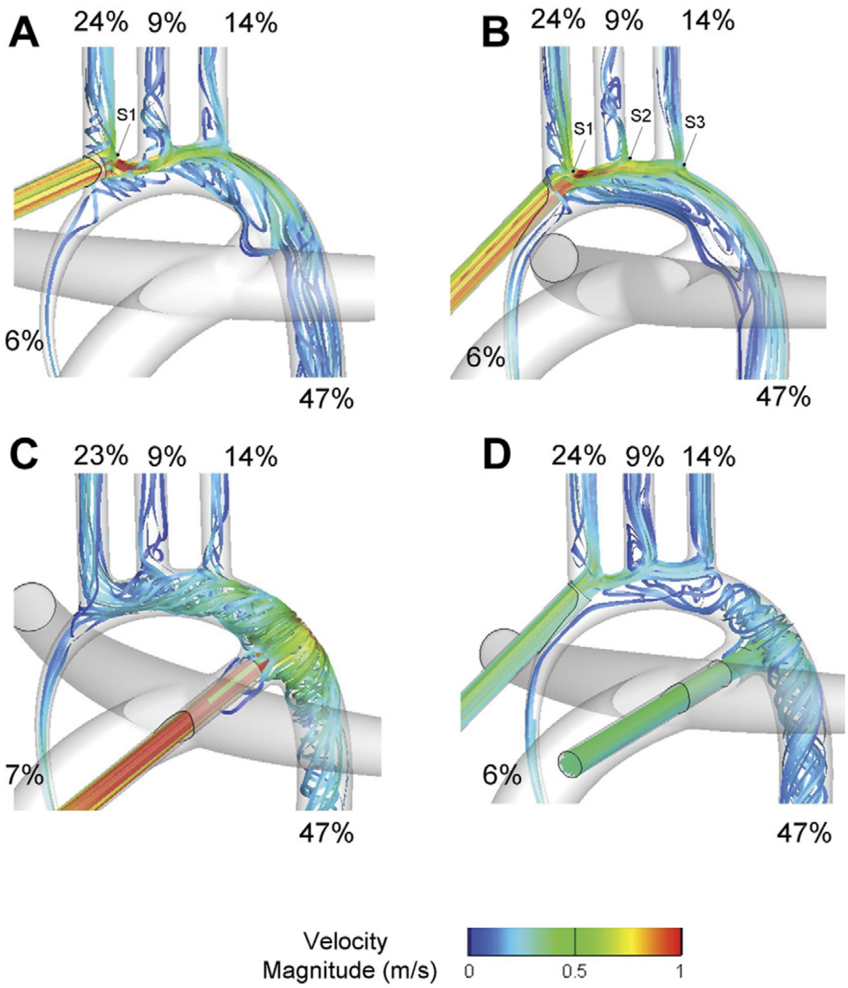

Fig 3. Comparison of the flow distributions and velocity fields associated with the four options for cannulation with pulmonary artery snaring, with S1, S2, and S3 representing flow-splitting points: (A) option 1; (B) option 2; (C) option 3; and (D) option 4.

In all options, blood flow to the coronaries is ensured through retrograde perfusion of the hypoplastic ascending aorta (6.3% to 6.6% of the flow). When the cannula was inserted into the innominate artery (option 1), blood flow impinged against the vessel wall opposite to the insertion point and was split between the innominate and the other vessels (point S1). The innominate artery received 24% of the blood, which is comparable to what was observed in the neonatal hypoplastic aorta with the PA snared. The remaining 70% of the blood flowed into the aortic arch, creating a flow detachment and a small recirculation region at the root of the left carotid artery. Although this could have a detrimental effect for the perfusion of the left carotid, the jet momentum here was small enough for the flow to curve around the detachment region and perfuse the left carotid. Flow recirculation regions were also noted at the root of the subclavian artery and along the inner wall of the aortic arch. Flow reattached in the descending aorta downstream of the PDA.

The flow structures observed when the cannula was approximately aligned with the axis of the ascending aorta (as in option 2) were fairly comparable to those observed in option 1, with the exception of the hemodynamics at the root of the innominate and left carotid artery. Blood split between the innominate and the outer wall of the aortic arch (point S1) and then impinged against the root of the left carotid (point S2) and subclavian arteries (point S3). These subsequent impingements allowed for a streamlined division of the blood flow between the different head and neck vessels.

The dynamics observed when inserting the cannula into the ductus (option 3) were drastically different. Blood impingement onto the aortic wall led to a complex helical flow pattern throughout the arch, allowing for the perfusion of all vessels with few regions of flow separation. In the dual cannulae approach (option 4), blood coming through the ductus mostly perfused the descending aorta, whereas blood entering the innominate root was mostly distributed to the head and neck vessels and coronaries. The resulting flow structures combine the characteristics of options 2 and 3.

Despite significantly different flow structures, the most striking characteristic of these results is that the resulting flow distributions are all in close range of one another (Table 1), closely reproducing the flow distributions of the neonatal hypoplastic configuration with the PA snared (see Control cases in Table 1).

Table 2. Flow Distributions Measured Across the Four Tested Cannulation Locations in the Verification Simulations[a]

Variable	Innominate	Left Carotid	Left Subclavian	Descending Aorta
Resistances, MPa.s.m^{-3}	524	1,307	849	163
Control, adult flow distribution, %	20	8	12	60
Flow distributions, %				
Option 1	34.5	2.7	10.9	52.0
Option 2	37.5	8.4	9.6	44.5
Option 3	17.7	7.4	11.6	63.3
Option 4	24.2	8.0	11.7	56.1

[a] Flow distributions were calculated as the percentage of perfusion flow rate with a perfusion flow rate of 4.5 L/min.

Effect of PA Snaring

To quantify the effect of PA snaring on cerebral perfusion, flow distributions measured in options 1 to 4 were compared with the preoperative flow distributions (ie, control case without the PAs snaring; Table 1). Considering only the distribution of the systemic flow rate [$\%_i = Q_i/(CO - Q_{LPA} - Q_{RPA})$], we obtained the following distributions in the preoperative configuration without snaring: 23.2%, 9.4%, 14.1%, 6.6%, and 46.8% for the innominate, left carotid, left subclavian, coronaries, and descending aorta, respectively. These values are exactly the ones obtained when snaring the PAs in the control case and are very close to the values measured in options 1 to 4, implying that the blood flow excluded from the pulmonary circulation through snaring is uniformly distributed to all systemic vascular beds.

Verification

As noted, although the cannula insertion location affected local hemodynamics, it had little effect on the resultant flow distributions. This finding may appear to contradict previous literature, such as the study of Kaufmann and colleagues [7], which reports a clear effect of even small cannulation variations. However, these studies were conducted for adult applications, implying different perfusion flow rates and downstream vascular resistances. To verify our approach, an additional set of simulations was thus conducted, seeking to reproduce the flow conditions of [7]. These simulations do not carry any direct relevance to DHCA but are rather meant to verify that the different cannulation options would have yielded different perfusion patterns under adult conditions. As in the Kaufmann and colleagues [7] study, coronary blood flow was neglected, the inflow rate was 4.5 L/min, and the mean aortic pressure was set to 60 mm Hg. Target systemic flow distributions and corresponding outflow resistances are provided in Table 2. These resistances correspond to an inferior and a global superior vascular resistance of 20 and 32 Woods units, respectively.

The flow fields and flow distributions obtained with the four options for cannulation, under adult flow conditions, are provided in Figure 4 and Table 2. The flow fields carry some resemblance to those observed in the DHCA simulations but with increased flow disturbances and larger flow separation regions due to the higher jet momentum. More remarkably, there were measurable differences in flow distributions. In option 1, the flow separation at the root of the left carotid obstructs the access to that vessel, which only receives 2.7% of the flow vs 8% in the reference case. Careful placement of the cannula, as in option 2, can help minimize this effect. Still, options 1 and 2 both led to a significant increase of the innominate blood flow of 34.5% or more compared with the reference value of 20%. In contrast, options 3 and 4 yielded flow distributions in closer match to the control values. Option 4 again combined the characteristics of options 2 and 3, inducing a slight increase in innominate flow rate (24.2% vs 20%) but still maintaining a proper perfusion of the lower systemic beds.

Comment

Although DHCA has played a central role in the development of surgical strategies to repair the aortic arch, it has concurrently been the subject of controversial discussions, with an increasing emphasis placed on the postoperative neurologic complications and significant nonneurologic morbidities. Multiple cannulation strategies have been discussed [3–5], seeking to ensure that all tissues are uniformly cooled, thereby minimizing the consequences of ischemia–reperfusion. Snaring the PAs (or the PDA) is also commonly used to try to increase systemic perfusion during the cooling process. However, it is difficult to quantify the efficacy of these strategies in vivo because it would require additional instrumentations in an already crowded and complex surgical space. As a result, neither the effect of the cannulation location nor that of PA snaring is properly understood. In this study, we compare three broad cannulation strategies—inserting a single cannula into the innominate artery (options 1 and 2) or into the PDA (option 3), or using 2 cannulae (option 4)—and quantify the benefits of PA snaring for each option.

Under neonatal conditions, all options lead to fairly comparable flow distributions, despite different hemodynamics. This is due to two combined factors: (1) the low momentum energy of the jet, due to the small perfusion flow rate (0.525 L/min), and more importantly, (2) the high neonatal vascular resistances. Indeed, blood flow to a given vessel in the domain of interest experiences two serial resistances—the internal resistance of the connec-

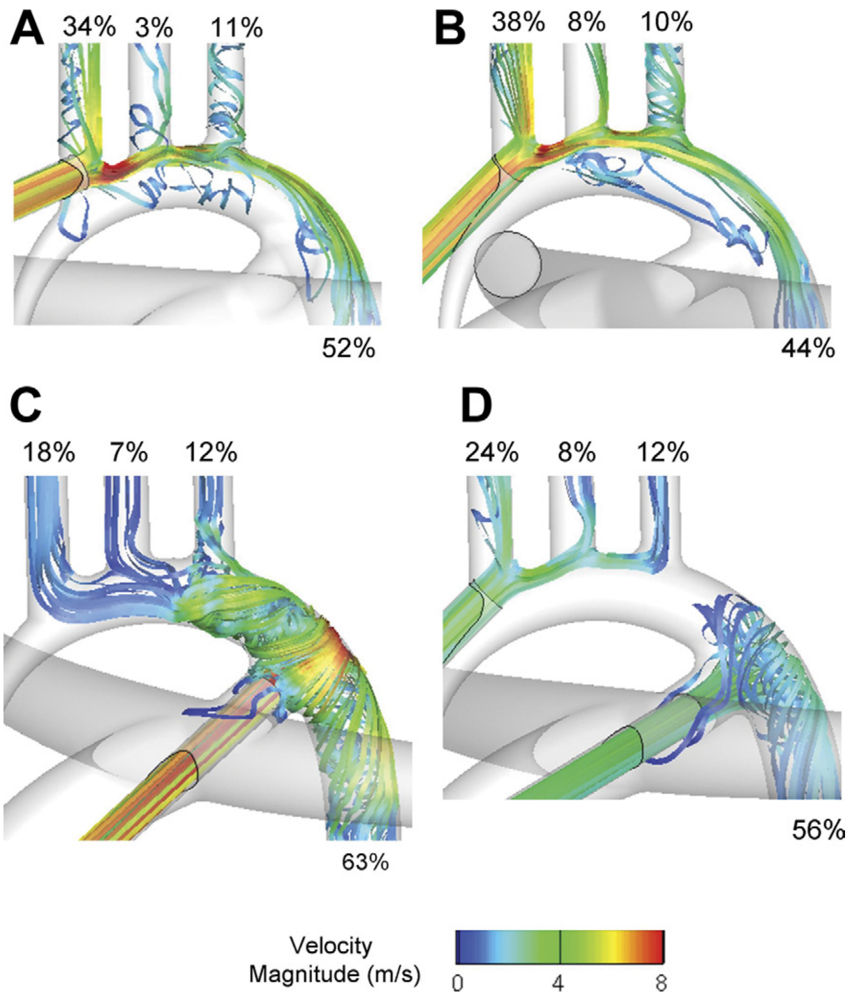

Fig 4. Comparison of the flow distributions and velocity fields associated with the four options for cannulation under "adult" flow conditions: (A) option 1; (B) option 2; (C) option 3; and (D) option 4.

tion (say the resistance encountered going from the cannula to the innominate outlet) and the resistance of the downstream vasculature. Because of the high neonatal vascular resistances imposed, the latter component dominates in all cases, leading to very low sensitivity to cannulation design. As an example, the internal resistance going from the cannula to the innominate was estimated to be 229 and 317 MPa.s.m^{-3} in options 1 and 3, respectively. The 88 MPa.s.m^{-3} difference was masked by the 2,370 MPa.s.m^{-3} downstream vascular resistance. Conversely, in the adult model of Kaufmann and colleagues [7] and our own validation case, the internal resistance was much higher (owing to higher flow disturbances because of the higher flow rates) and the downstream resistances were much lower, making the cannula placement and orientation a much more critical consideration.

These findings are of major clinical importance because they imply that in neonatal patients without further aortic arch complications, the surgeon should be able to use the cannulation strategy of his or her choice and yet achieve the flow distributions dictated by the downstream vascular resistances. In addition, comparison of the flow distributions with PA snaring to the control without snaring demonstrates that snaring the PAs benefits all systemic vascular beds equally; that is, the amount of blood flow derived from the pulmonary circulation into a given vascular bed will be proportional to the resistance of that vascular bed. In particular, if some vascular beds become constricted faster than others, due to the effect of vasoconstrictors or to cooling, their resistance will increase and the distribution of the cold blood will be rerouted toward the vascular beds with a lower resistance (including those that have received vasodilators).

However, three things are important to keep in mind: First, the relative insensitivity to the cannulation approach only holds true under neonatal conditions and not under adult conditions.

Second, in all presented options, the cannula(e) only slightly protruded into the vessel and thereby did not obstruct flow toward any of the systemic vessels. However, if a cannula was inserted more deeply, it could obstruct the flow and increase the local resistance, which could in turn influence the overall flow distributions. As an example, perfusion through a Gore-Tex conduit (W. L. Gore and Associates, Flagstaff, AZ) sewn to the innominate presents the advantage that it will not obstruct the innominate artery in any way, whereas a direct cannulation to that vessel should be performed without inserting the cannula too deeply. Similarly, cannulation into the ascending aorta carries the risk that part of the retrograde perfusion of the coronaries will be blocked if the hypoplastic ascending aorta is not sufficiently larger than the cannula.

Third, along the same lines, the aortic geometry presented here featured an aorta that was hypoplastic but otherwise normal. In particular, it did not feature any aortic coarctation, which is present to some degrees in about half of the HLHS patients. For options 1, 2, and 3, any increase in resistance in the isthmus of the coarctation will bias flow toward the upper or lower body, depending on the point of insertion of the cannula. As illustrated in Figure 3, the 2-cannulae approach (option 4) allows blood to be supplied upstream and downstream of the coarctation, thereby minimizing the effect of the coarctation resistance and ensuring that the resultant flow distributions do not significantly deviate from their physiologic values. Although a dual-cannulation approach is routinely used for patients with severe coarctation, having two independent blood sources may also provide an advantage for patients with mild coarctation as soon as there is a measurable arm–leg pressure difference, reflecting a significant increase in the isthmus resistance. Future work should incorporate varying degrees of aortic coarctation to assess the effectiveness of using 2 cannulae and quantify the effect of different cannula insertion depths into the ascending aorta and innominate artery.

This study has some limitations. Idealized approaches are a perfect setting to conduct preliminary investigations, narrowing the number of variables to only those that seem to have the largest impact. Still, the relevance of the associated findings should be carefully considered. The simplified neonatal aortic arch used in this model was designed after a careful review of the available literature and anatomic data. Furthermore, the different scenarios envisioned were meant to capture the effect of largely different strategies. The absence of differences between those scenarios implies that small changes in the local geometry are likely to have a minor, nonmeasurable impact on the measured performances.

Beyond the geometric simplifications, the downstream vasculatures are modeled by a fixed set of normalized resistances, whereas in vivo, these vascular resistances may vary with progressive hypothermia. As discussed, this will have a direct effect on the flow distribution, redistributing the blood flow to the least constricted vessels. However, the variation of vascular tone during cardiopulmonary bypass and hypothermic cooling is not well understood. The next step would thus be to conduct concurrent clinical and computational investigations to enable more detailed modeling and correlate the two modalities.

In conclusion, this study sought to determine the cannulation strategy that will best distribute blood flow and to characterize the benefits of PA snaring during DHCA in HLHS patients. The relative resistance of the different vascular beds was the strongest determinant for the flow distributions during cooling in neonates due to the particularly high resistance of the neonatal vascular beds. As a consequence, the cannulation strategy had little impact on the global performance in patients without aortic coarctation or other vessel stenosis, allowing the surgeon to use the method he or she prefers (1 or 2 cannulae, location and angle of insertion). Patients with an aortic coarctation will most likely present an exception to that rule and benefit from a 2-cannulae approach (option 4). Future work should thus incorporate varying degrees of aortic coarctation to assess the effectiveness of using 2 cannulae and varying cannula insertion depth.

This study was supported by the National Heart, Lung and Blood Institute Grant HL-67622.

References

1. Wypij D, Newburger JW, Rappaport LA, et al. The effect of duration of deep hypothermic circulatory arrest in infant heart surgery on late neurodevelopment: the Boston Circulatory Arrest Trial. J Thorac Cardiovasc Surg 2003;126:1397–403.
2. Okita Y, Ando M, Minatoya K, Kitamura S, Takamoto S, Nakajima N. Predictive factors for mortality and cerebral complications in arteriosclerotic aneurysm of the aortic arch. Ann Thorac Surg 1999;67:72–8.
3. Tchervenkov CI, Korkola SJ, Shum-Tim D. Surgical technique to avoid circulatory arrest and direct arch vessel cannulation during neonatal aortic arch reconstruction. Eur J Cardiothorac Surg 2001;19:708–10.
4. Gerdes A, Joubert-Hubner E, Esders K, Sievers HH. Hydrodynamics of aortic arch vessels during perfusion through the right subclavian artery. Ann Thorac Surg 2000;69:1425–30.
5. Poirier NC, Drummond-Webb JJ, Hisamochi K, Imamura M, Harrison AM, Mee RB. Modified Norwood procedure with a high-flow cardiopulmonary bypass strategy results in low mortality without late arch obstruction. J Thorac Cardiovasc Surg 2000;120:875–84.
6. Joubert-Huebner E, Gerdes A, Sievers HH. An in vitro evaluation of a new cannula tip design compared with two clinically established cannula-tip designs regarding aortic arch vessel perfusion characteristics. Perfusion 2000;15:69–76.
7. Kaufmann TA, Hormes M, Laumen M, et al. The impact of aortic/subclavian outflow cannulation for cardiopulmonary bypass and cardiac support: a computational fluid dynamics study. Artif Organs 2009;33:727–32.
8. Pekkan K, Dur O, Sundareswaran K, et al. Neonatal aortic arch hemodynamics and perfusion during cardiopulmonary bypass. J Biomech Eng 2008;130:061012.
9. Pekkan K, Dasi LP, Nourparvar P, et al. In vitro hemodynamic investigation of the embryonic aortic arch at late gestation. J Biomech 2008;41:1697–706.
10. Ilbawi AM, Spicer DE, Bharati S, Cook A, Anderson RH. Morphologic study of the ascending aorta and aortic arch in hypoplastic left hearts: surgical implications. J Thorac Cardiovasc Surg 2007;134:99–105.
11. Wang C, Pekkan K, de Zelicourt D, et al. Progress in the CFD modeling of flow instabilities in anatomical total cavopulmonary connections. Ann Biomed Eng 2007;35:1840–56.
12. Walther FJ, Siassi B, Ramadan NA, Ananda AK, Wu PY. Pulsed Doppler determinations of cardiac output in neonates: normal standards for clinical use. Pediatrics 1985;76:829–33.
13. Lagana K, Balossino R, Migliavacca F, et al. Multiscale modeling of the cardiovascular system: application to the study of pulmonary and coronary perfusions in the univentricular circulation. J Biomech 2005;38:1129–41.