Catheter-Directed Thrombolysis for Occluded Central (Ascending Aorta-to-Pulmonary Artery) Shunts: Importance of Shear Stress-Induced, Platelet-Mediated Thrombosis

Thrombolysis and Shear Stress in Central Shunts

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Abstract

A central (ascending aorta-to-pulmonary artery) shunt is a standard palliative operation for infants with cyanotic congenital heart disease. Thrombosis of these shunts can be life-threatening. We report our experience with catheter-directed thrombolysis using recombinant tissue plasminogen activator to locally treat totally occluded central shunts as an alternative to surgery. Ten patients (median age 47 days) successfully underwent the procedure. Following thrombolysis, shunt patency was verified by angiography. The arterial oxygen (O_2) saturations in 100% O_2 increased from a median value of 55% to 90%. Major bleeding did not occur in any patients. Computational fluid dynamics was used to identify a relationship between shunt hemodynamics and thrombosis. We retrospectively analyzed blood flow through simulations of these shunts as they would have appeared prior to obstruction. The calculations revealed that flow negotiating "angulated" portions of these central shunts produced wall shear stresses of 157–168 Pa (or N/m²), with shear rates reaching 31,400–33,600/s. These values are easily high enough to initiate platelet activation/aggregation, leading to thrombus formation.

We conclude that: 1) catheter-directed thrombolysis can be used to rapidly, effectively, and safely resolve total central shunt occlusion in critically ill neonates and 2) central shunts containing prominent angulation are at risk for developing shear stress-induced, platelet-mediated thrombosis. This finding is clinically important as this flow-directed process is not affected by prophylactic aspirin against shunt thrombosis.

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Key Words

Occluded central shunts • Wall shear stress • Thrombosis • Shunt thromboylysis

Introduction

Central (ascending aorta-to-pulmonary artery) shunts have been the standard initial surgical management for many infants and young children with cyanotic congenital heart disease [1-10]. These shunts (polytetrofluoroethylene tubular grafts) are favored

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as they generally promote good growth of small pulmonary arteries with minimal vessel distortion [4, 11-12]. However, central shunts have been associated with a high incidence of thrombosis [13-15], which can be a life-threatening or even fatal complication of the procedure. It is, therefore, imperative to rapidly diagnose and effectively treat clotting of a shunt. Shunt thrombosis has traditionally been surgically managed by placing a new graft, although this approach does entail a significant risk to the patient, especially severely ill infants.

In adult patients, percutaneous catheter-directed thrombolysis (CDT) using fibrinolytic agents is increasingly being used as an alternative to surgery to hasten clot resolution in cases of systemic vascular obstruction [16-19]. Typically, this procedure entails infusing thrombolytic drugs, most commonly recombinant tissue plasminogen activator (rTPA or alteplase) directly into the occluded vessel, as an effective treatment to re-establish patency with minimal side effects. Accordingly, specific practice guidelines regarding the use of CDT have been established [20-22]. In contrast, evidence-based recommendations for this form of therapy in infants and young children are not available, and current practice is largely based on previously reported cases [23-28]. Thus, part I of this study consisted of a review of our experience with a cohort of critically ill infants who developed complete central shunt thrombosis. Catheter-based rTPA delivery directly into the shunts was used to relieve the obstructions.

We recently used computational fluid dynamics (CFD) to demonstrate that a viscous fluid (e.g., blood) traversing an "angulated" vessel (or conduit) can produce marked increases in fluid shear stress near the luminal wall (i.e., wall shear stress) where platelets tend to reside [29]. Moreover, it is known that high fluid shear stress can activate platelets, causing them to aggregate and/or bind to coagulation proteins in the blood to form microparticles that serve as precursors for thrombus formation [30]. The shunts considered in this study required an extended length and prominent angulation to connect them from the anterior surface of the ascending aorta to the more posteriorly oriented pulmonary artery (Figure 1). Given this anatomical arrangement, we rationalized that central shunts containing prominent angulation
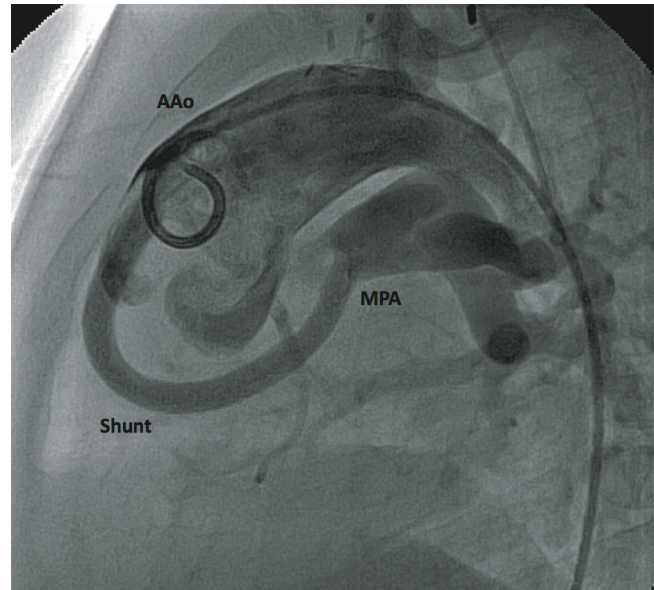

Figure 1. Angiogram performed in the ascending aorta showing an aorta to main pulmonary artery shunt in lateral view. The shunt arose off the anterior surface of the ascending aorta and was then angulated inferiorly and posteriorly to complete the connection to the main pulmonary artery. AAo = ascending aorta; MPA = main pulmonary artery.

would be at risk for shear stress-induced, platelet-mediated thrombosis. In part II of this investigation, we explored this possibility using: 1) patient-specific angiograms to construct computer simulations of representative central shunts in part I, as they would have appeared prior to becoming obstructed, and 2) CFD to determine whether flow through these angulated shunts could produce wall shear stresses of sufficient magnitude to promote platelet activation/aggregation. Our goal was to identify a relationship between shunt hemodynamics and thrombosis. An understanding of shear stress-mediated thrombosis is clinically important as this process does not involve thromboxane A_2 production and hence is insensitive to aspirin (ASA) [29, 31].

Methods

In part I of this study, we conducted a search of the institutional medical database to identify patients treated with percutaneous CDT to relieve central shunt obstruction between 2008 and 2014. The patients presented with marked arterial blood hemoglobin oxygen (O_2) desaturation and echocardiographic Doppler flow evidence for total shunt occlusion. Once determined, the patients were taken to the cardiac catheter-

ization suite where the diagnosis was angiographically con-firmed. Infusion of rTPA directly into (or near) the shunt was the primary intervention performed. The institutional proto-col for rTPA administration, which is based on a study by Wang et al. [32], was used as a guide to initiate thrombolytic therapy.

All cases were approached retrograde via the aorta. Typi-cally, shunts were engaged by passing a 4-French (F) end-hole catheter over a 0.018-inch guidewire. If the guidewire could not be positioned in the shunt to the operator's satisfaction, the rTPA was initially administered at the mouth of the shunt. In some patients, if the angiographic appearance of the shunt suggested residual clot following thrombolysis, shunt angio-plasty was performed with a (4 mm × 20 mm) Sterling balloon catheter (Boston Scientific, Marlborough, MA, USA). For one patient in extremis, the balloon catheter was used to mechan-ically advance the clot distally, to at least hasten arterial satu-ration improvement. The rTPA was then delivered to the distal portion of the shunt and/or the pulmonary arteries until there was angiographic resolution. Care was taken not to dislodge clot into the aorta.

The amount and mode of rTPA delivery to the shunt were based on the extent of thrombus formation, response to the drug, urgency to relieve the obstruction, and prior experience of the physician conducting the procedure. All patients under-went mechanical ventilation with a fraction of inspired O_2 of 1.0 (100%). Each individual received (100 U/kg) of intravenous heparin. Typically, boluses (0.1 – 0.5) of TPA were given over 5 to 10 minutes with the catheter positioned within or at the orifice of the shunt. Generally, an rTPA dose is not influenced as much by the patient's weight as by the sizes of the shunt

and clot, as well as the response achieved. Occasionally, rTPA was diluted in normal saline to a concentration of (0.5 mg/mL) and infused at a specific rate when a more extended period of time (15–30 min) was desired to administer the drug. Inter-mittent hand injections of contrast material were periodically used to assess clot resolution progression. Thrombolytic suc-cess was defined as restoration of blood flow through the graft with (>95%) patency as evidenced by angiography. Successful thrombolysis was achieved in all the patients. Following the procedure, patients were placed on an intravenous infusion of heparin at a median dose of 15 U/kg/h.

In part II of this study, CFD was used to assess wall shear stress magnitude and flow distribution through representa-tive central shunts (cases 2 and 4) in part I, as all shunts pos-sessed a similar degree of prominent angulation. Angiograms were performed after thrombolysis to delineate the anatomic features of the unobstructed shunt pathways. The simulated central shunts were constructed using a 3D modeling soft-ware computer package (Autodesk Inventor, San Rafael, CA, USA). Once the centerline of a shunt was determined from the angiogram, a constant-diameter, circular cross-section was swept along its course to form the tubular graft (Figure 2, case 2; Figure 3, case 4) [29].

The flow calculations were carried out using the CFD com-puter program Fluent 14.5 (Ansys, Inc., Lebanon, NH, USA), which solves the 3-D Navier-Stokes and continuity equations using the finite volume method [29, 33]. The fluid was assumed to be of Newtonian character, with a density of 1,060 kg/m^3 and a viscosity of 5×10^{-3} kg/m–s (hematocrit ~40%). The no-slip, zero-flow velocity, boundary condition was imposed
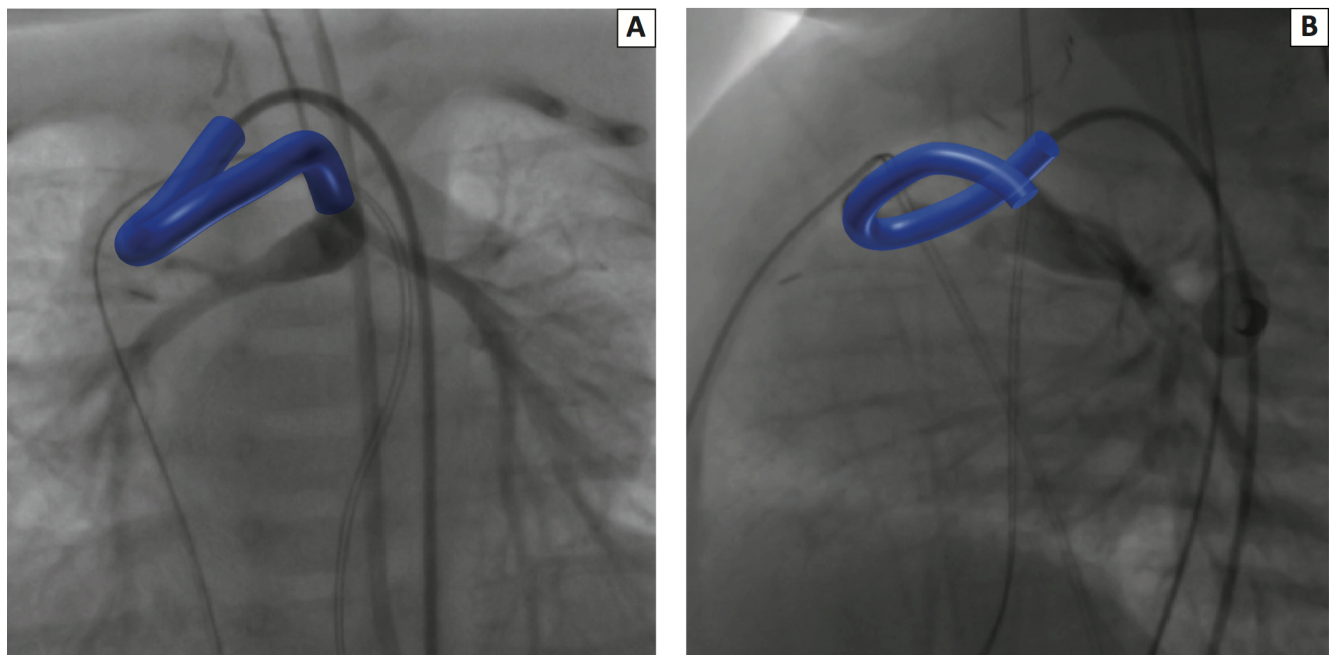
Figure 2. Computer simulation of an ascending aorta to main pulmonary artery shunt (blue) superimposed on the angiogram for case 2 (see Table 1). The shunt is 3.5 mm in diameter and contains prominent curvature. (*Panel A*) Anterior and (*Panel B*) lateral views. Catheter is 4F.
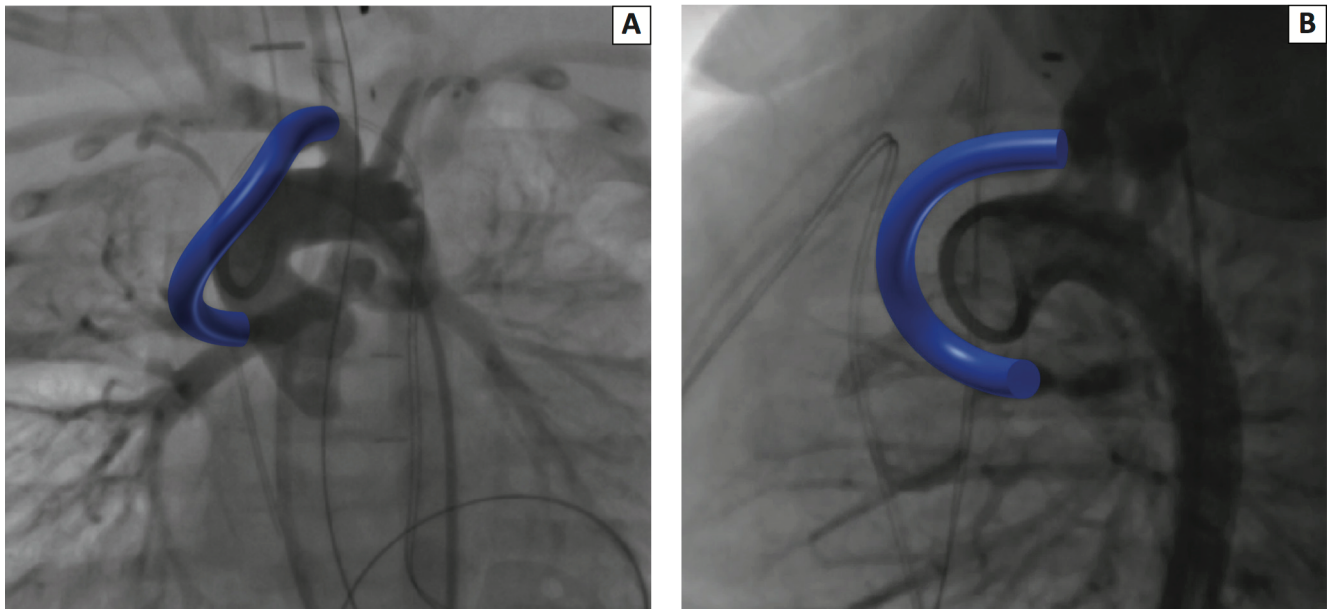
Figure 3. Computer simulation of an innominate artery to right pulmonary artery shunt (blue) superimposed on the angiogram for case 4 (see Table 1). The shunt is 3.5 mm in diameter and contains prominent curvature. (*Panel A*) Anterior and (*Panel B*) lateral views. Catheter is 4F.

at the luminal wall. For simplicity, steady flow was considered. The overall pressure drop (mean ascending aorta or innominate artery pressure minus mean pulmonary artery pressure) was taken as 6,667 N/m² (50 mm Hg) [29]. Shear stress, which represents the force (per unit area) exerted by flow on the luminal surface of a vessel (or conduit), is expressed in units of pressure (Pascals-Pa or N/m²). For a Newtonian fluid, the shear rate is the ratio of (*Shear Stress* (N/m²)/*Viscosity* (kg/m-s)) and carries units of (1/s).

Results

In part I of this study, we assessed the efficacy of using CDT, with rTPA, to treat complete central shunt occlusion. The clinical diagnosis of the patients' congenital heart disease, type of shunt employed and drugs used as prophylaxis against shunt thrombosis, are presented in Table 1. All the shunts that underwent CDT had at least one prominent curvature based on the way they were initially crafted. In 70% of the cases, the shunts arose off the anterior surface of the ascending aorta and then curved inferiorly and posteriorly to complete the anastomosis to the pulmonary artery. The shunts ranged from 3.0–4.0 mm in diameter. ASA alone was used in most (70%) cases as an antiplatelet agent against thrombosis; ASA plus

dipyridamole was used in one case, and continuous intravenous heparin infusion was being delivered at the time of thrombosis in two cases (Table 1). Table 2 lists the patients' weights in kilograms (kg) and ages in days (d) at the time of the thrombolysis procedure, as well as the time (d) from shunt placement to thrombosis and the total amounts of rTPA in (mg/kg) required to resolve the thrombi.

Thrombolytic success was defined as restoration of blood flow through the shunt with no residual thrombus on angiography. The median time from shunt placement to thrombosis was 19 d (range, 1–47 d). All patients were still in the hospital when their shunts obstructed. The median amount of rTPA required to resolve the thrombus was 0.3 mg/kg (range, 0.18–5.75 mg/kg). The quantity of rTPA required for CDT varied depending on the patient's weight and the extent of thrombus formation. The systemic arterial hemoglobin O_2 percent saturation (by pulse oximetry) increased dramatically, from a median value of 55% to 90%, following thrombolysis. There were three cases in which the thrombus extended beyond the shunt; namely, into the innominate artery (case 4), left pulmonary artery (LPA, case 5), or right pulmonary artery (RPA, case 9). In

Table 1:   Cardiac diagnosis, type of central shunt and diameter (mm) and drug used as prophylaxis against shunt thrombosis.

Case	Cardiac diagnosis	Type of shunt and diameter (mm)	Prophylaxis
1a	TS, hypoplastic RV, valvular PS S/P balloon pulmonary valvuloplasty	Asc Ao to MPA (3.5)	ASA
1b	Same	Same	Same
2	TOF, sub PS, hypoplastic RPA and LPA	Asc Ao to MPA (3.5)	ASA
3	TS, hypoplastic RV, sub PS, S/P augmentation of RVOT	Asc Ao to MPA (3.0)	ASA
4	TA, hypoplastic RV, restrictive VSD, sub PS	Proximal Innominate Artery to RPA (3.5)	ASA
5	Dextrocardia, unbalanced AVC, PA, supracardiac TAPVR (heterotaxia)	Asc Ao to LPA (3.5)	ASA
6	TOF with PA	Asc Ao to MPA (3.5)	ASA and dipyridamole
7	TA, hypoplastic RV, restrictive VSD, sub PS S/P balloon atrial septostomy	Asc Ao to MPA (3.0)	ASA
8	DORV, VSD, sub PS	Asc Ao to MPA (3.5)	Heparin infusion
9	PA, VSD, systemic arterial collateral vessels, hypoplastic native RPA and LPA	Right subclavian artery to RPA (modified Blalock-Taussig shunt) (4.0)	Heparin infusion

TS = tricuspid stenosis; TA = tricuspid atresia; PS = pulmonary stenosis; PA = pulmonary atresia; S/P = status post; RV = right ventricle; RVOT = right ventricular outflow tract; Asc Ao = ascending aorta; MPA = main pulmonary artery; RPA = right pulmonary artery; LPA = left pulmonary artery; VSD = ventricular septal defect; AVC = atrioventricular canal; TOF = tetralogy of Fallot; DORV = double outlet right ventricle; TAPVR = total anomalous pulmonary venous return; ASA = aspirin.

these cases, the additional clot was dissolved as part of the overall thrombolysis procedure. The largest quantity of rTPA (5.75 mg/kg or a total of 21.8 mg) was required in case 4, as the thrombus had extended from the shunt through the innominate artery to the origin of the right carotid and right subclavian arteries. The total rTPA infusion time was 88 min. The clots in the LPA (case 5) and RPA (case 9) were in close proximity to the pulmonary ends of their corresponding shunts.

In five of the cases, a (4 mm × 20 mm) Sterling balloon catheter (Boston Scientific) was used to strip the luminal surface of the graft of any residual clot. In all cases, free flow through the shunts was confirmed by angiography (Figures 4 and 5). Major bleeding, defined as the need for a blood transfusion, did not occur in any of the patients. Although several of the patients received thrombolysis soon after shunt placement, no bleeding occurred at the surgical or catheterization sites. There were no serious complications associated with or following the thrombolysis procedure. There have been no deaths in this group of patients.

In part II of the study, we constructed computer simulations of a representative ascending aorta to main pulmonary artery (MPA) shunt (Figure 2, case 2) and of an innominate artery to RPA shunt (Figure 3, case 4) based on their corresponding post-thrombolysis angiograms. We numerically determined wall shear stress (and shear rate) throughout the simulated shunts and pulmonary arteries. Each studied shunt was 3.5 mm in diameter. For case 2, the calculated flow rate was 1.6×10^{-5} m³/s (1 L/min). The corresponding contour plot of wall shear stress is presented in Figure 6. The distribution of wall shear stress is complex for this convoluted blood flow pathway; it reached its maximum value (168 Pa or N/m², red), with a shear rate of (33,600/s), on the side walls of the shunt where curvature (the apex) is most prominent. The wall shear stress downstream from the apex remained elevated at (80 or N/m², green) with a shear rate of (16,000/s), and it attained a secondary maximum (110 Pa or N/m², light green) with a shear rate of (22,000/s). In contrast, an area of low shear stress (10 Pa or N/m², dark blue) with a shear rate of (2,000/s) was also identified, providing an environ-

Table 2: Patient data associated with the thrombolysis procedures. The columns contain the: weights, in kilograms (kg), and ages, in days (d), at the time of the procedure; time, in days (d) from shunt placement to shunt thrombosis.; total amount of rTPA, in mg/kg, required to resolve the thrombus, and arterial blood O_2 saturations (%) pre- and post-procedure. Additional procedures, see text.

Case	Weight (kg)	Age (d)	Time (d) from shunt placement to thrombosis	Total rTPA (mg/kg) to resolve the Thrombus	Additional procedures	Pre rTPA arterial saturations (%)	Post rTPA arterial saturations (%)
1a	5.0	54	28	0.2	None	50	80
1b	5.1	75	21	0.3	None	50	80
2	3.0	34	12	0.66	None	60	80
3	2.8	55	41	0.71	Balloon (20 x 4 mm) of shunt	60	80
4	3.8	18	12	5.75	None	60	90
5	3.0	40	13	0.2	Balloon (20 x 4 mm) of shunt	40	90
6	3.5	24	17	0.28	Balloon (20 x 4 mm) of shunt	70	90
7	3.3	69	47	0.18	Balloon (20 x 4 mm) of shunt	50	90
8	1.5	34	27	1.66	Balloon (20 x 4 mm) of shunt	50	90
9	7.9	385	1	0.26	None	70	90
Median	**3.4**	**47**	**19**	**0.29**		**55**	**90**

rTPA = recombinant tissue plasminogen activator.

ment for flow recirculation.

For case 4, the calculated flow rate was 1.9×10^{-5} m³/s (1.2 L/min). The corresponding contour plot of wall shear stress is shown in Figure 7. It reached its maximum value of (157 or N/m², orange), with a shear rate of (31,400/s), on the side walls of the shunt, where curvature is most prominent. The wall shear stress downstream from the apex remained high at (80 or N/m², green) with a shear rate of (16,000/s) due to persistent angulation of the graft. For both of these cases, if the shunts are considered to be "straight tubes" of equivalent diameter and length, wall shear stress is dramatically reduced to 30 N/m², emphasizing the importance of graft curvature.

Discussion

Many infants and young children with cyanotic congenital heart disease are highly dependent on the distribution of blood flow between the systemic and pulmonary circulations. Thrombosis of a central shunt can, therefore, be a serious complication, with potentially grave consequences. The clinical presentation of shunt thrombosis is often acute and requires urgent treatment to restore critically needed blood flow to the lungs. Of concern, however, is that the use of systemically administered thrombolytic agents relatively soon after surgical placement of a shunt could lead to serious bleeding at surgical sites or elsewhere. Thus, our goal using CDT was to rapidly deliver rTPA into the clotted shunt, so its action on systemic
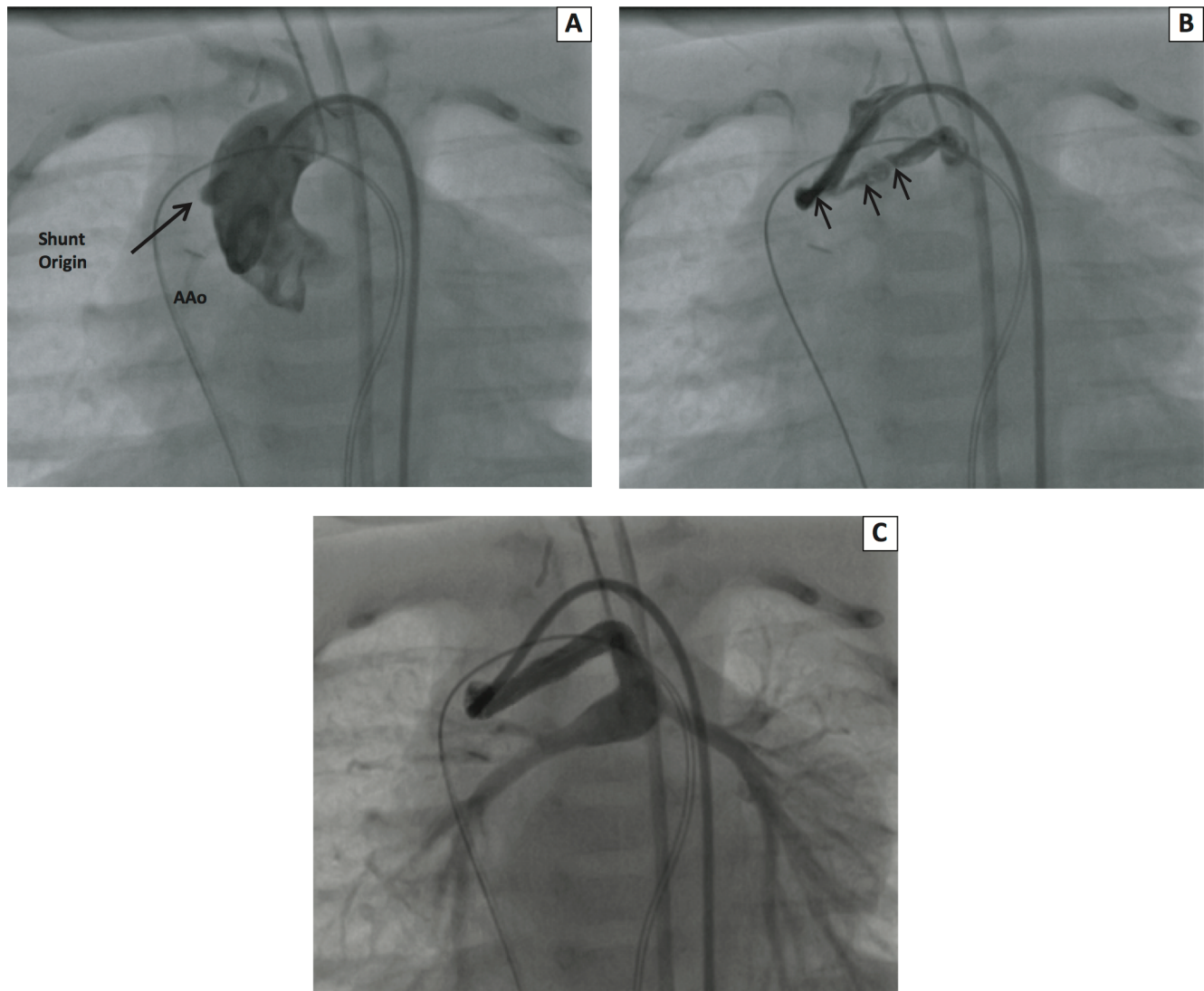
Figure 4. Angiograms during phases of CDT with rTPA for case 2 in the anterior view (also see Figure 2). *Panel A.* Complete shunt occlusion by thrombus (pre-rTPA). Shunt origin from the ascending aorta (arrow). Note the slight protuberance of the ascending aorta. *Panel B.* Partial resolution with residual thrombus (arrows). *Panel C.* Complete resolution of thrombus (post-rTPA). The catheter is 4F. AAo = ascending aorta; CDT = catheter-directed thrombolysis; rTPA = recombinant tissue plasminogen activator.

circulation would be limited.

An important aspect of part I of this study was to demonstrate that CDT with rTPA can be used to resolve even complete central shunt thrombosis in critically ill infants, with minimal side effects. The median amount of rTPA required to dissolve the thrombus in the graft was 0.3 mg/kg; the corresponding median infusion time was 30 min (range, 2–88 min), which would correspond to a rate of 0.6 mg/kg/h. This amount of rTPA is about half the

recommended loading dose of this drug if given systemically [34]. In general, however, the total amount of rTPA required for a thrombolysis procedure will depend on the extent of the thrombus formation, response to the drug, coagulation status of the patient, and complications associated with the procedure. There are several case reports on the local administration of rTPA to treat thrombosis of modified Blalock-Taussig shunts [28, 35-37]. In these cases, resolution of the clotted grafts was achieved
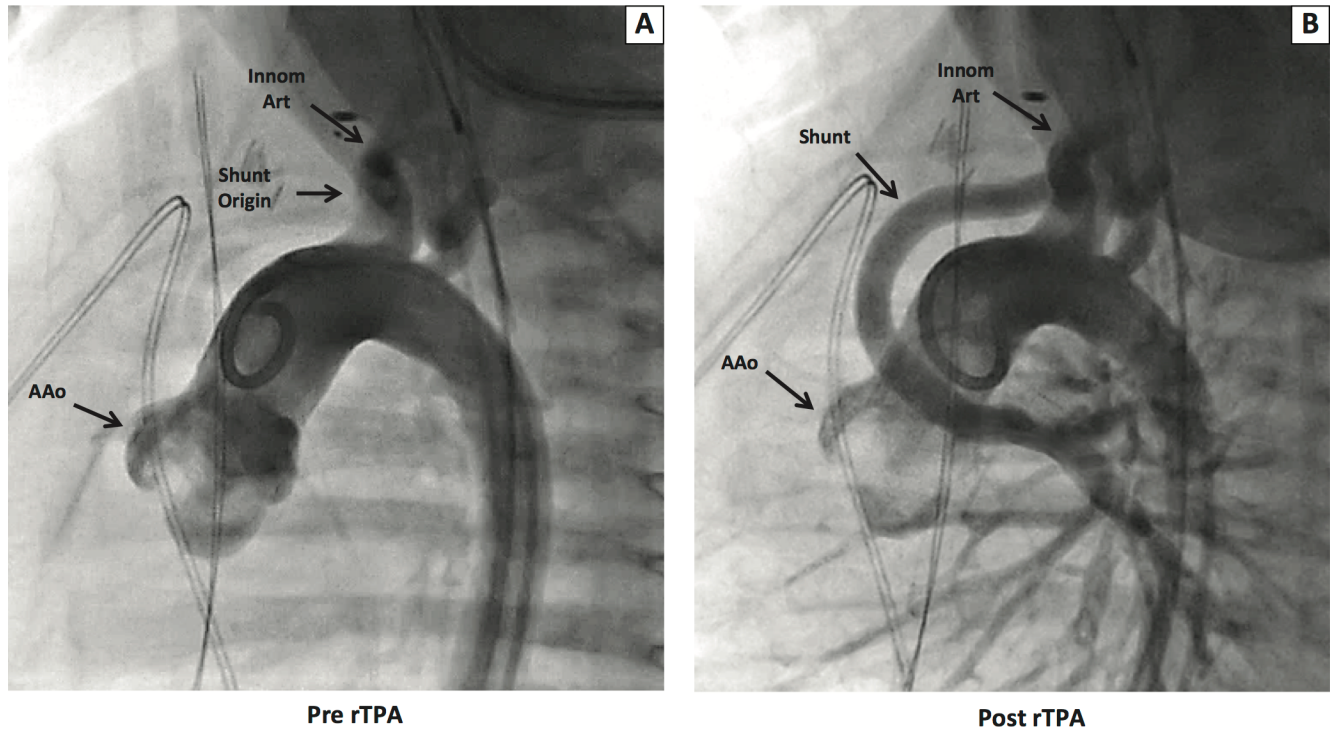
Figure 5. Angiograms pre- and post-CDT with rTPA for case 4 in lateral view (see also Figure 3). *Panel A*. Complete shunt occlusion by thrombus (pre-rTPA). Shunt origin from the innominate artery (arrow). *Panel B*. Complete resolution of thrombus (post-rTPA). The catheter is 4F. AAo = ascending aorta; CDT = catheter-directed thrombolysis; Innom Art = innominate artery; rTPA = recombinant tissue plasminogen activator.

without hemorrhagic complications.

In part II of this study, we sought to identify a relationship between central shunt hemodynamics and thrombus formation. When a viscous fluid flows through a vessel (or conduit), it imparts a force (per unit area) on the luminal surface; the so-called wall shear stress. For a Newtonian fluid, wall shear stress directly depends on the fluid's viscosity and its shear rate at the vessel (or conduit) wall, where platelets tend to reside. The interaction of blood flow shearing forces with platelet surfaces is considered the primary mechanical factor responsible for initiating pathologic thrombosis in the arterial system. High shear stress (or shear rate) induces conformational changes in platelet membrane glycoproteins. These changes facilitate the binding of fibrinogen and von Willebrand factor to these glycoproteins, ultimately creating complexes that lead to clot formation [38-40]. For example, Holme et al. [30] showed that blood platelets become activated and form procoagulant microparticles through aggregation when exposed to a shear stress of 50 N/m^2,

with a shear rate of 10,500/s. Ruggeri et al. [41] reported that platelets can undergo aggregation, even independent of activation, at a higher shear stress of 80 N/m^2, with a shear rate of 20,000/s.

In case 2 of part I of this study, wall shear stress reached 168 Pa (or N/m^2) with a shear rate of 33,600/s at the position of maximum curvature in the graft. Likewise, in case 4, wall shear stress at the greatest curvature rose to 157 Pa (or N/m^2), with a shear rate of 31,400/s. These shear stresses (and shear rates) are easily high enough to support platelet-mediated thrombus formation. We previously demonstrated that increases in wall shear stress encountered when flow traverses a prominent bend or curve in a vessel (or conduit), as shown in red in Figure 6 and orange in Figure 7, arise as a consequence of reactive centrifugal effects creating patterns of recirculating flow in the cross-sectional plane of the tube [29, 42-44]. This fluid motion can organize into spiral flow fields that, in their rotational motion, augment local shearing
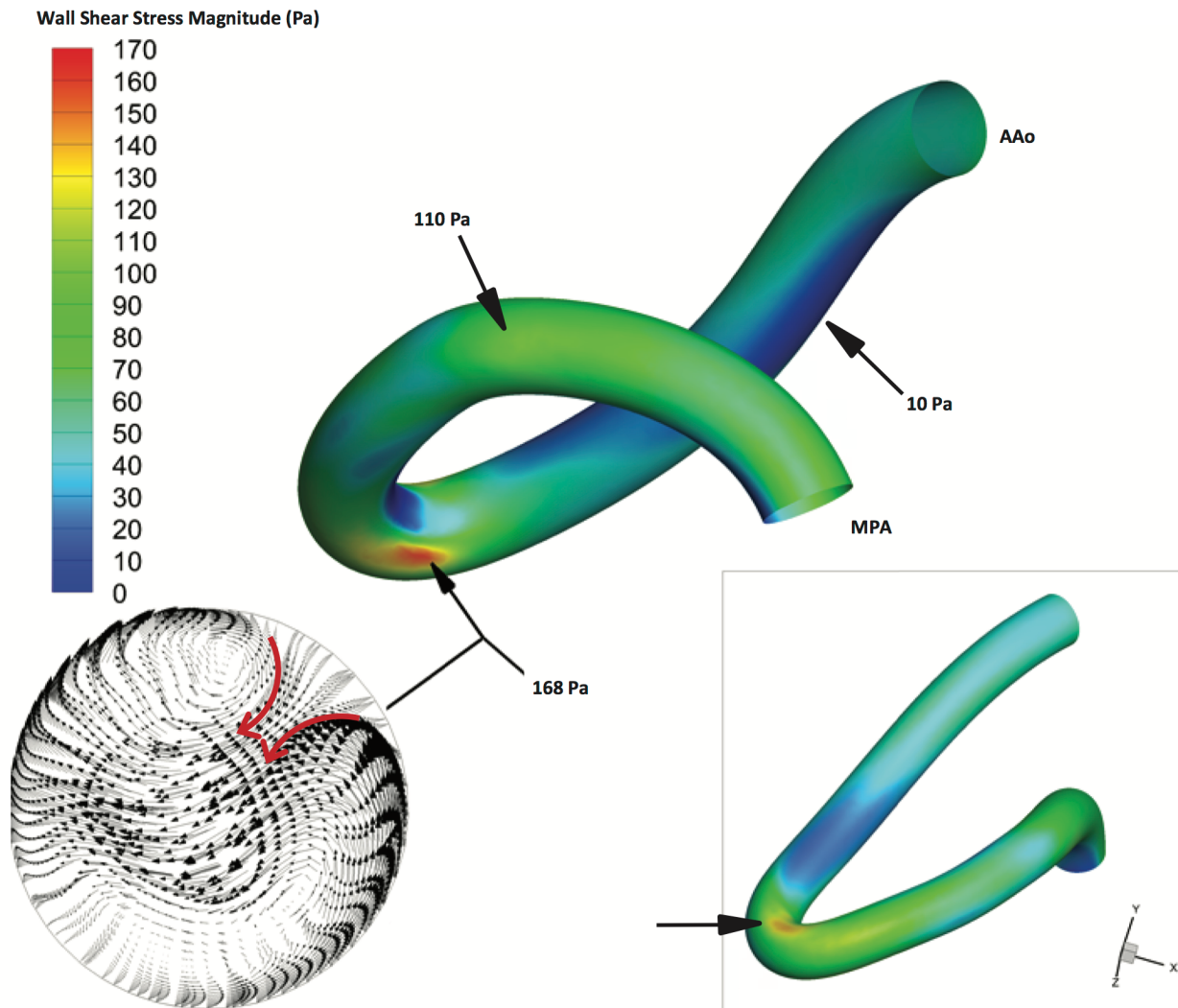
Figure 6. The upper part of the figure shows the wall shear stress contour plot for case 2 in the text (see Figure 2). The shunt has been rotated to better show the regions of high wall shear stress. The maximum wall shear stress (168 Pa or N/m², red) is on the side wall of the shunt (arrow). A secondary maximum in wall shear stress (110 Pa or N/m², light green) is indicated by another arrow. An area of low wall shear stress (10 Pa or N/m², dark blue) runs along the underside of the shunt (arrow). The lower right side of the figure shows a similar region of high wall shear stress on the contralateral side wall of the shunt (arrow). The lower left side of the figure shows the flow velocity distribution in the cross-sectional plane perpendicular to the central axis of the shunt, in the region of highest wall shear stress. The velocity vectors are projected onto the cross-sectional plane (small dark arrows). The two counterrotating vortices underlie the regions of high wall shear stress, where curvature in the shunt is greatest. The direction of rotation of the fluid composing the vortices is indicated (bold red arrows). AAo = ascending aortic (proximal) end of the shunt; MPA = main pulmonary artery (distal) end of the shunt.

forces on the walls of the tube (see the lower left portions of Figures 6 and 7). In doing so, a hemodynamic process is established that facilitates platelet activation/aggregation.

The surgical approach at our institution is to construct rather long and angulated shunts (Figures 1, 2, and 3) from the anterior surface of the ascending aorta to the more posteriorly
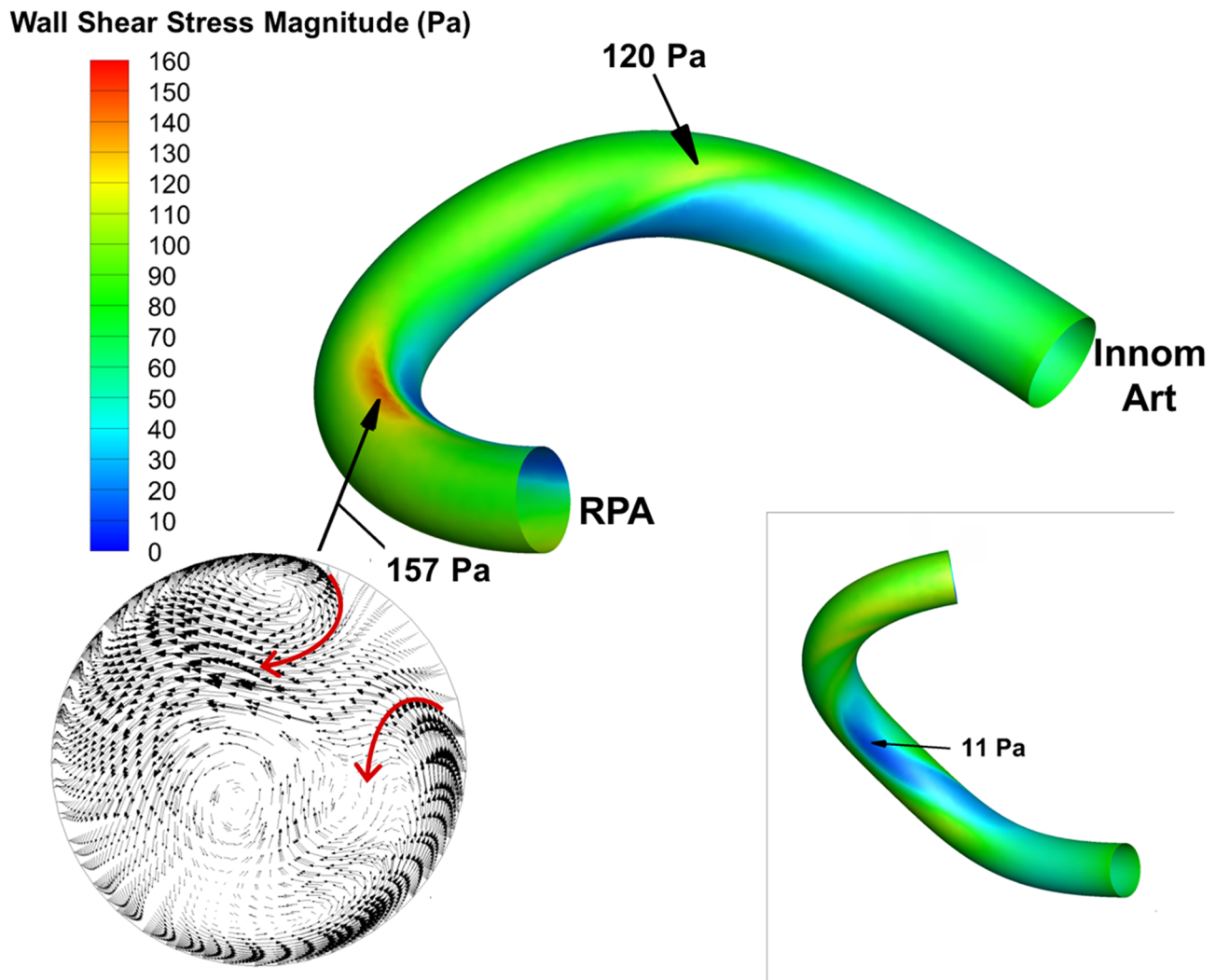
Figure 7. The upper part of the figure shows the wall shear stress contour plot for case 4 in the text (see Figure 3). The shunt has been rotated to better show the regions of high wall shear stress. The maximum wall shear stress (157 Pa or N/m^2, red) is on the side wall of the shunt (arrow). A secondary maximum in wall shear stress (120 Pa or N/m^2, yellow/green) is indicated by another arrow. The lower right side of the figure shows an area of low wall shear stress (11 Pa or N/m^2, dark blue) that runs along the undersurface of the shunt (arrow). The lower left side of the figure shows the flow velocity distribution in the cross-sectional plane perpendicular to the central axis of the shunt in the region of highest wall shear stress. Velocity vectors are projected onto the cross-sectional plane (small dark arrows). The two counterrotating vortices underlie the regions of high wall shear stress, where curvature in the shunt is greatest. The direction of rotation of the fluid composing the vortices is indicated (bold red arrows). Innom Art = innominate artery (proximal) end of the shunt, RPA = right pulmonary artery (distal) end of the shunt.

oriented pulmonary artery. This type of shunt may lessen pulmonary overcirculation, as most of our patients do not require anticongestive management. However, as demonstrated in a previous study [29] and here, central shunts containing prominent angulation are a risk factor for shear stress-induced platelet-mediated thrombosis. Therefore, contrary to the previous practice of employing ASA alone as prophylaxis against shunt thrombosis, ASA now is being used in conjunction with dipyridamole to prevent clotting [29]. The efficacy of this approach remains to be delineated

as the hemodynamic substrate fostering high shear stress remains. An alternative surgical approach would be to surgically construct relatively short shunts with minimal curvature, as in modified Blalock-Taussig shunts. This approach should provide adequate relief for the relatively short time periods currently required for initial palliation.

Conclusion

CDT with rTPA can be used to rapidly resolve central shunt thrombosis in infants and young children, even in the early postoperative period, with minimal side effects. Although this combined clinical and numerical study is limited by the small numbers of patients, our success using CDT to resolve complete central shunt obstruction is encouraging. This procedure appears to be a good therapeutic option to avoid the risks associated with urgent surgery in infants. Moreover, by employing computer simulations of fluid flow through angulated central shunts, we identified a hemodynamic process likely responsible for thrombosis. This mechanism may well be involved in other aorta-to-pulmonary artery shunt occlusions. Prominent changes in fluid direction from shunt angulation and the consequent centrifugal effects on flow through the vessel (or conduit), can create vortices leading to increases in the local wall shear stress (and sheer rate) of sufficient magnitude to initiate platelet activation/aggregation and ultimately thrombus formation. Given that neither the cyclooxygenase pathway nor thromboxane A_2 production is involved in this hemodynamic process, ASA alone will provide insufficient protection against clotting.

Acknowledgment

Conflict of Interest

The authors have no conflict of interest relevant to this publication.

Comment on this Article or Ask a Question

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