Publish Date:
June 2016
Volume 2, Issue 3

JSHD

Journal of Structural Heart Disease

OFFICIAL JOURNAL OF THE PICS FOUNDATION

PICS Foundation

PEDIATRIC AND ADULT INTERVENTIONAL CARDIAC SYMPOSIUM

Published by
Science International Corp.
ISSN 2325-4637

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JSHD
Journal of Structural Heart Disease

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Journal of Structural Heart Disease (ISSN 2325-4637) is an online open-access journal issued bi-monthly (6 issues per year, one volume per year) by Science International Corporation.

All correspondence should be directed to: Ziyad M. Hijazi, MD, Editor-in-Chief, Journal of Structural Heart Disease, PO Box 26999, Doha, Qatar. Tel.: +974-4003-6601, E-Mail: jshd@scienceinternational.org

JSHD
Journal of Structural Heart Disease

Original Research Article

Journal of Structural Heart Disease, June 2016,
Volume 2, Issue 3:67-78
DOI: http://dx.doi.org/10.12945/j.jshd.2016.002.15

Received: March 23, 2015
Accepted: June 16, 2015
Published online: June 2016

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

Dhiraj Singh, MD[1,2], Steffan Sernich, MD[1,2], Ernest Siwik, MD[1,2], Nancy Ross-Ascuitto, MD[1,3], Carey Celestin, MS[4], Robert Ascuitto, PhD, MD[1,3]

[1] Division of Pediatric Cardiology, Department of Pediatrics, Louisiana State University Health Sciences Center, New Orleans, Louisiana, USA

[2] Division of Cardiology, Children's Hospital of New Orleans, New Orleans, Louisiana, USA

[3] Division of Cardiology, Louisiana State University Healthcare Network, New Orleans, Louisiana, USA

[4] Department of Mechanical Engineering, University of New Orleans, New Orleans, Louisiana, USA

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/m^2), 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.

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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E-Mail: jshd@scienceinternational.org
http://structuralheartdisease.org/

© 2016 Journal of Structural Heart Disease
Published by Science International Corp.
ISSN 2326-4004

Accessible online at:
http://structuralheartdisease.org/

* Corresponding Author:
Robert Ascuitto, PhD, MD
Louisiana State University Healthcare Network
Division of Cardiology
3700 St. Charles Ave., New Orleans, LA 70115, USA
Tel.: +1 504 884-0660; E-Mail: nrossascuitto@yahoo.com

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 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].

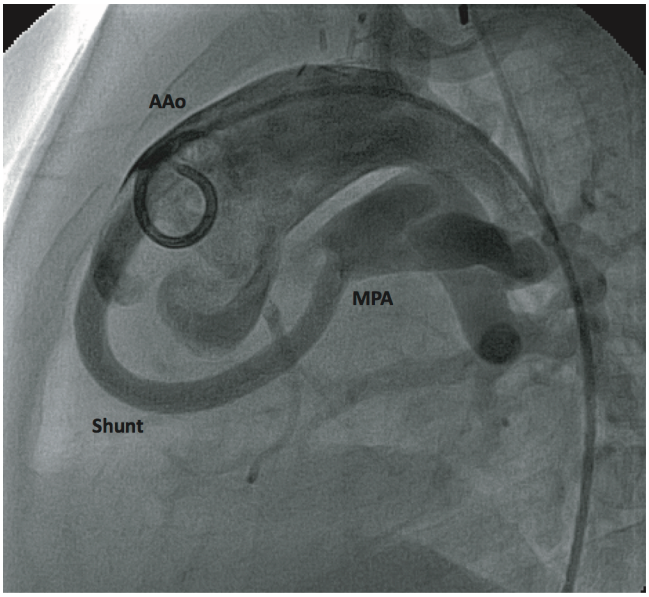

Figure 1. Angiogram performed in the ascending aorta showing an aorta to main pulmonary artery shunt in lateral view. The shunt arose off the anterior surface of the ascending aorta and was then angulated inferiorly and posteriorly to complete the connection to the main pulmonary artery. AAo = ascending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

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 confirmed. Infusion of rTPA directly into (or near) the shunt was the primary intervention performed. The institutional protocol 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. Typically, 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 angioplasty 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 mechanically advance the clot distally, to at least hasten arterial saturation 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 underwent 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. Intermittent hand injections of contrast material were periodically used to assess clot resolution progression. Thrombolytic success 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 representative central shunts (cases 2 and 4) in part I, as all shunts possessed 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 software 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 computer 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

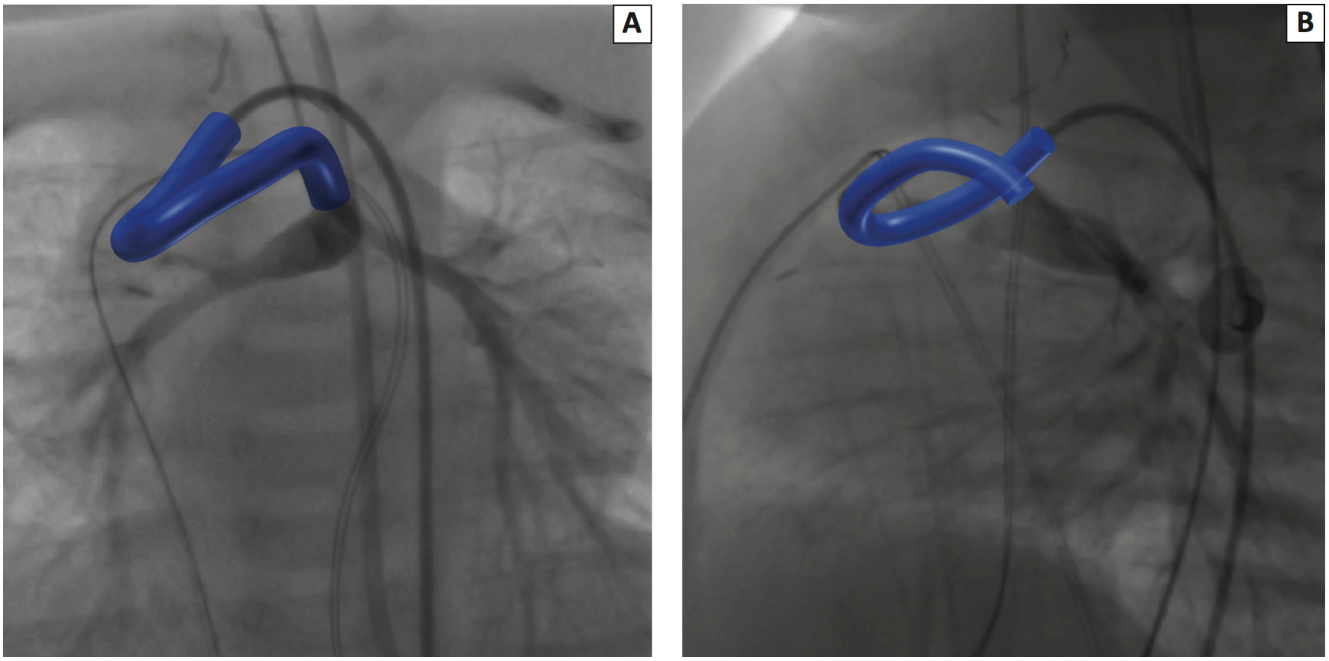

Figure 2. Computer simulation of an ascending aorta to main pulmonary artery shunt (blue) superimposed on the angiogram for case 2 (see Table 1). The shunt is 3.5 mm in diameter and contains prominent curvature. (*Panel A*) Anterior and (*Panel B*) lateral views. Catheter is 4F.

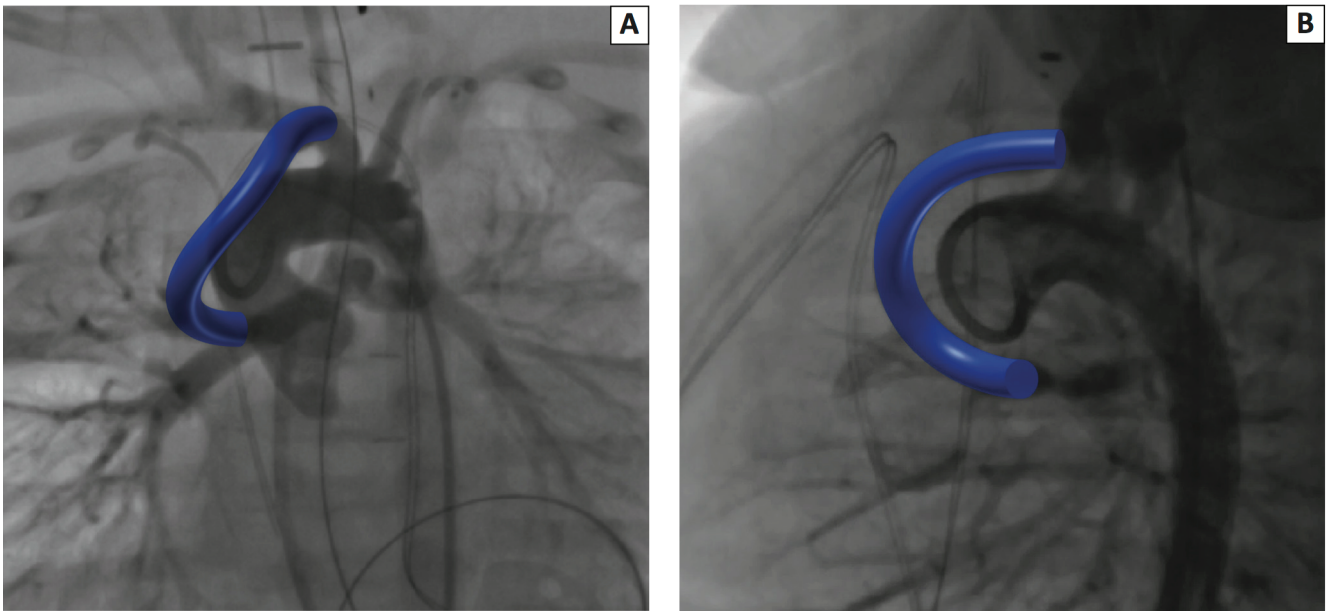

Figure 3. Computer simulation of an innominate artery to right pulmonary artery shunt (blue) superimposed on the angiogram for case 4 (see Table 1). The shunt is 3.5 mm in diameter and contains prominent curvature. (*Panel A*) Anterior and (*Panel B*) lateral views. Catheter is 4F.

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/m^2 (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/m^2). For a Newtonian fluid, the shear rate is the ratio of (*Shear Stress* (N/m^2)/*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} m^3/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/m^2, 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/m^2, green) with a shear rate of (16,000/s), and it attained a secondary maximum (110 Pa or N/m^2, light green) with a shear rate of (22,000/s). In contrast, an area of low shear stress (10 Pa or N/m^2, 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} m^3/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/m^2, 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/m^2, 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/m^2, 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

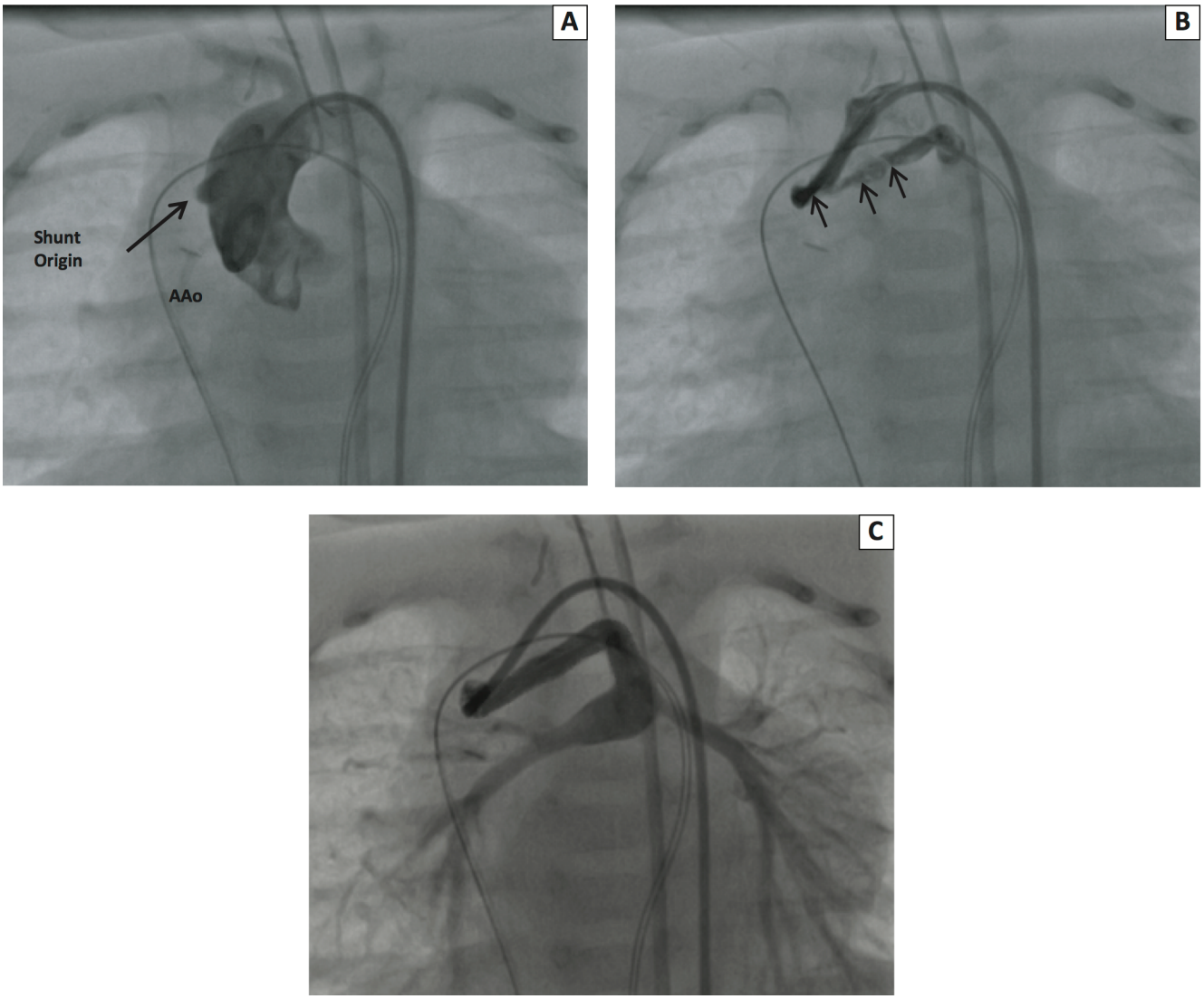

Figure 4. Angiograms during phases of CDT with rTPA for case 2 in the anterior view (also see Figure 2). *Panel A*. Complete shunt occlusion by thrombus (pre-rTPA). Shunt origin from the ascending aorta (arrow). Note the slight protuberance of the ascending aorta. *Panel B*. Partial resolution with residual 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

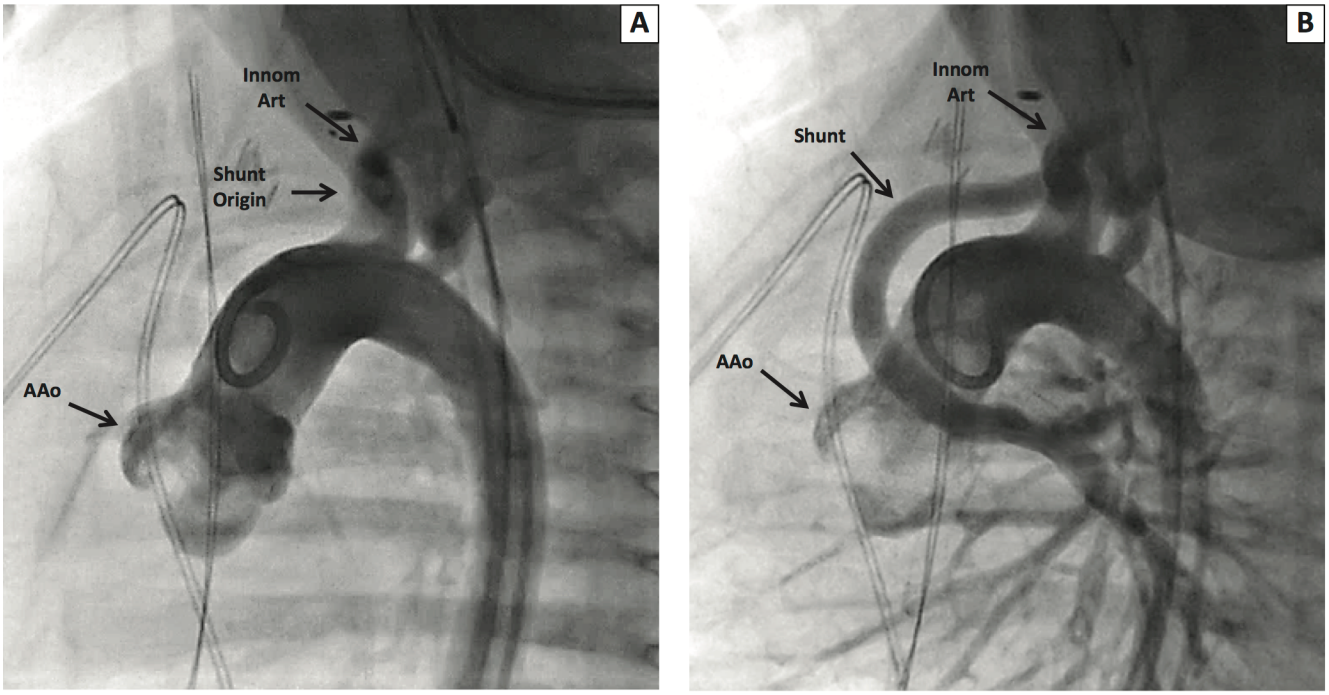

Figure 5. Angiograms pre- and post-CDT with rTPA for case 4 in lateral view (see also Figure 3). *Panel A*. Complete shunt occlusion by thrombus (pre-rTPA). Shunt origin from the innominate artery (arrow). *Panel B*. Complete resolution of thrombus (post-rTPA). The catheter is 4F. AAo = ascending aorta; 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

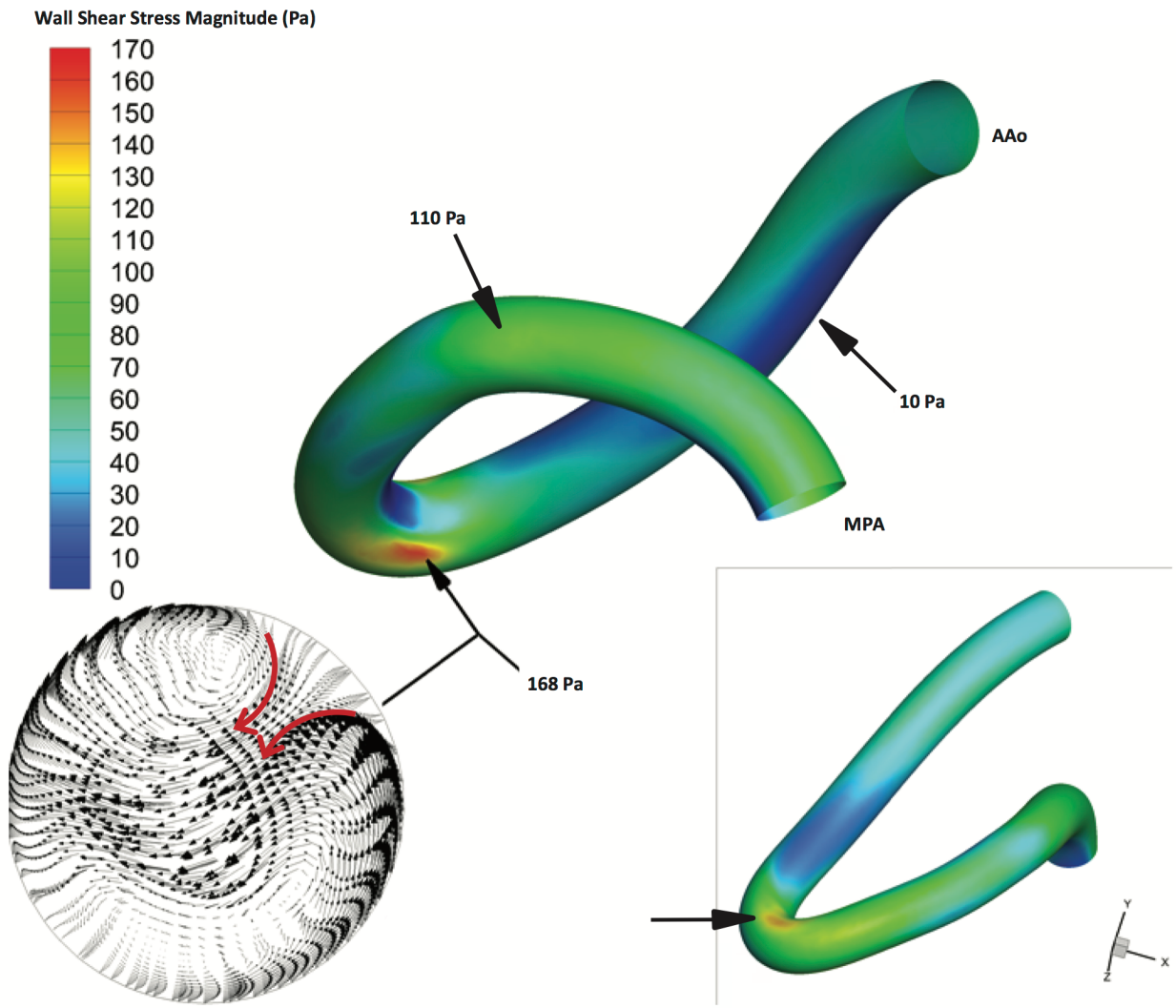

Figure 6. The upper part of the figure shows the wall shear stress contour plot for case 2 in the text (see Figure 2). The shunt has been rotated to better show the regions of high wall shear stress. The maximum wall shear stress (168 Pa or N/m^2, red) is on the side wall of the shunt (arrow). A secondary maximum in wall shear stress (110 Pa or N/m^2, light green) is indicated by another arrow. An area of low wall shear stress (10 Pa or N/m^2, 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

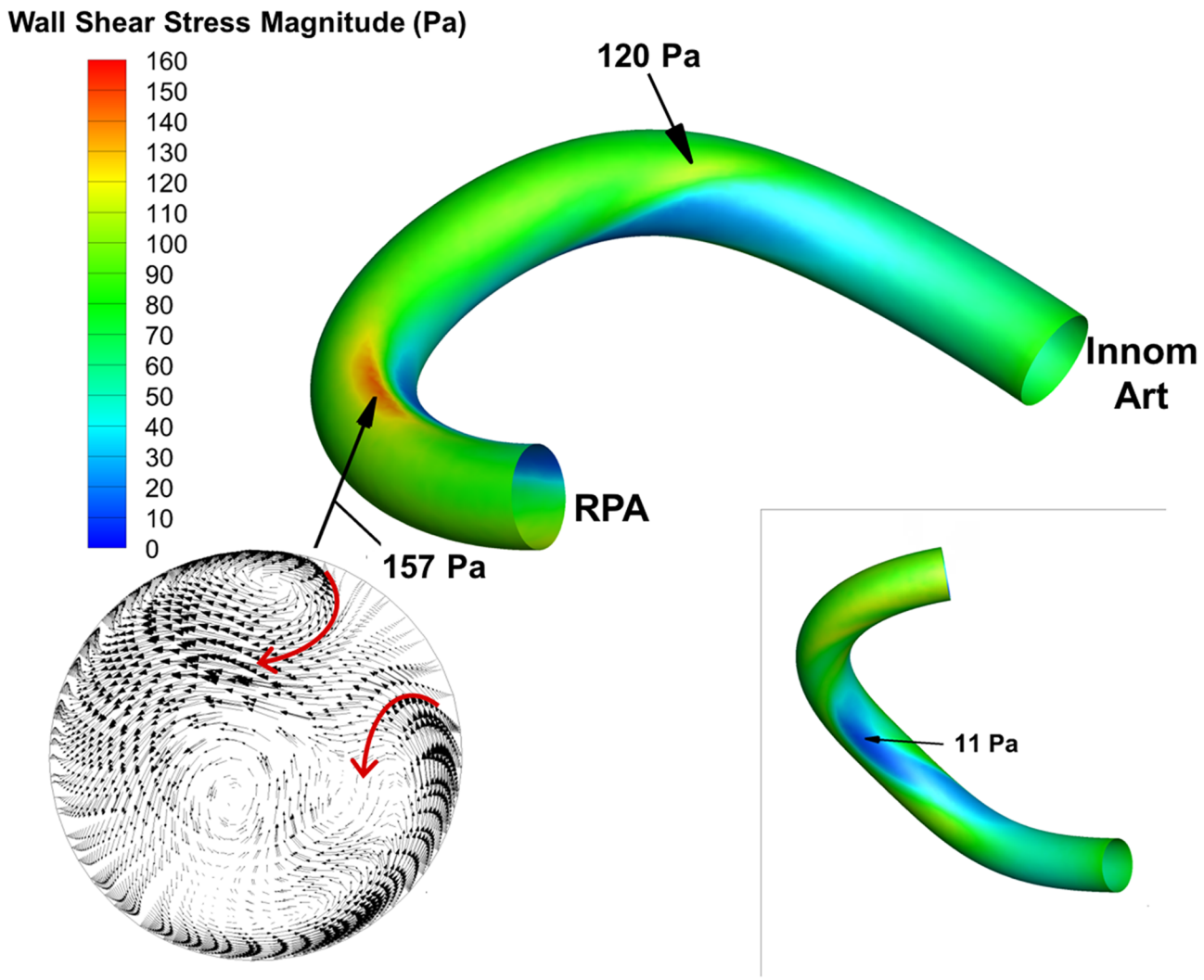

Figure 7. The upper part of the figure shows the wall shear stress contour plot for case 4 in the text (see Figure 3). The shunt has been rotated to better show the regions of high wall shear stress. The maximum wall shear stress (157 Pa or N/m^2, red) is on the side wall of the shunt (arrow). A secondary 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

This work was supported in part by a Board of Regents Grant from the State of Louisiana (LSE-QF-RD-A-18 Support Fund).

Conflict of Interest

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

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Cite this article as: Singh D, Sernich S, Siwik E, Ross-Ascuitto N, Celestin C, Ascuitto R. Catheter-Directed Thrombolysis for Occluded Central (Ascending Aorta-to-Pulmonary Artery) Shunts: Importance of Shear Stress-Induced, Platelet-Mediated Thrombosis. Journal of Structural Heart Disease. 2016;2(3):67-78. DOI: http://dx.doi.org/10.12945/j.jshd.2016.002.15

JSHD
Journal of Structural Heart Disease

Original Research Article

Journal of Structural Heart Disease, June 2016,
Volume 2, Issue 3:79-86
DOI: http://dx.doi.org/10.12945/j.jshd.2016.003.15

Received: June 19, 2015
Accepted: July 26, 2015
Published online: June 2016

Extended Application of Self-Fabricated Covered Stents for Interventions in Adults with Congenital Heart Disease

Subeer K. Wadia, MD[1*], Damien Kenny, MB, MD[2], Wail Alkashkari, MB, MD[3], Thomas Matella, RT(R)(CV)[4], Clifford J. Kavinsky, MD, PhD[5], Ziyad M. Hijazi, MD, MPH, MSCAI[6]

[1] Ronald Reagan UCLA Medical Center, Internal Medicine, Los Angeles, California, USA

[2] Division of Pediatric Cardiology, Our Lady's Children's Hospital, Dublin, Ireland

[3] King Faisal Cardiac Center, Jeddah, Saudi Arabia

[4] Rush University Medical Center, Chicago, Illinois, USA

[5] Rush University Medical Center, Division of Cardiology, Chicago, Illinois, USA

[6] Sidra Medical and Research Center, Doha, Qatar

Abstract

Background: **Covered stents are widely used outside of the United States to treat adult patients with congenital heart disease. However, these stents have not been approved by the United States Food and Drug Administration (FDA). We describe our experience with large diameter, self-fabricated covered stents for patients with congenital heart disease.**

Methods: **We retrospectively examined results of adults with congenital heart disease who received a self-designed covered stent at our institution. We detailed our method of fabricating the covered stent and modifications in delivery to minimize traction or trauma against the outer covering of the stent.**

Results: **We implanted 25 fabricated covered stents in 21 patients. The cohort was divided into three disease groups: coarctation of the aorta [group (a), n = 17], pulmonary artery or right ventricle-to-pulmonary artery conduit stenosis [group (b), n = 3], and right-to-left shunting at site of prior anastomosis [group (c), n = 1]. In group (a), the mean systolic pressure gradient was reduced from 35.5 mm Hg to 5.7 mm Hg ($p < 0.001$). In group (b), the mean stenotic pressure gradient decreased from 37.7 to 8.7 mm Hg. The patient in group (c) had obliteration of shunting and improvement in symptoms.**

Conclusions: **Our self-fabricated covered stents were safe and provided effective gradient reduction or intraluminal continuity to treat individualized lesions related to congenital heart disease. Covered stents increase the therapeutic options for the interventional cardiologist and in some cases may be safer for the patient. There needs to be increased pressure from providers towards the FDA to approve these stents in the United States.**

Key Words

Covered stent • Self-fabricated • Congenital heart disease • Adults

Introduction

Covered stents are widely being studied as adjunctive or alternative therapeutic options in interventional cardiology [1-4]. Due to the intraluminal continuity afforded by expanded polytetrafluoro-

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E-Mail: jshd@scienceinternational.org
http://structuralheartdisease.org/

© 2016 Journal of Structural Heart Disease
Published by Science International Corp.
ISSN 2326-4004

Accessible online at:
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* Corresponding Author:
Damien Kenny, MB, MD
Rush Center for Congenital & Structural Heart Disease
Department of Cardiology
1650 W. Harrison St, Chicago, IL 60612, USA
Tel.: +1 312 942 6800; Fax: +1 312 942 5869; E-Mail: damien_Kenny@rush.edu

ethylene (ePTFE) covering, there is growing interest for their use in adults with congenital heart disease (ACHD), particularly in high risk older patients with severe or heavily calcified stenotic lesions [5, 6]. The most recent population based studies from Finland and Norway demonstrated the aging population of complex congenital heart disease resulting from improved early surgical interventions [7, 8]. As such, we will continue to witness a higher rate of highly individualized late term consequence of palliative surgeries in adults with complex heart disease [9, 10]. Interventional cardiology in ACHD must mature to provide safe and effective options for this already aging population.

Unfortunately, at present there are no large diameter covered stents approved for use in the United States. However, there are clinical trials ongoing examining the safety of such covered stents. The United States Food and Drug Administration (FDA) has allowed commercially made covered stents, such as the covered Cheatham-Platinum stent (CCPS), to be used on limited basis for emergency or compassionate use in select centers (personal communication, NuMED, Inc.). This handicap not only limits the data on safety and efficacy, but also restricts availability of the stent in standard catheterization laboratories, which are already treating adults with complex heart disease across the country.

In this study, we describe our innovative technique of handcrafting individualized covered stents as an approach to provide a safe and therapeutic option while circumventing the hurdle of commercial availability for transcatheter interventions in ACHD. Specifically, we describe our experience of fabricating covered stents using bare metal stents and ePTFE in the catheterization laboratory with our subsequent immediate and follow up results in a cohort of patients with coarctation of the aorta (CoA), pulmonary artery (PA) or right ventricle-to-pulmonary artery (RV-PA) conduit stenosis, and right-to-left shunt secondary to baffle leak.

Patients and Methods

Over a 12-year period (from August 2001 to August 2013), we retrospectively identified 21 patients who received a self-designed covered stent for a lesion related to congenital heart disease. We divided the cohort of patients into three subgroups: (a) patients with CoA (n = 17), (b) PA or RV-PA conduit stenosis (n = 3), and (c) right-to-left shunt secondary to baffle anastomosis leak (n = 1). We subsequently performed detailed analysis of the self-fabricated covered stent cohort data, including angiography and follow-up computed tomography (CT).

The median and mean differences in pre- and post-stent gradients for groups (a) and (b) were analyzed using Wilcoxon matched pairs signed ranks test and paired *t* test analysis, respectively, on Microsoft Excel® (Microsoft, Redmond, Washington). Pulse oximetry and New York Heart Association (NYHA) Classification for Heart Failure were used to assess evolution of symptoms.

Stent Fabrication

Our method of fabricating the covered stent has been previously described [11]. In short, bare metal stents of appropriate length and diameter were selected. Ten patients had MAX-LD or MEGA-LD stents (ev3, Plymouth, Minnesota), six patients had PG Genesis stents (Cordis Corporation, Warren, New Jersey), and five patients received Palmaz stents (Cordis Corporation, Warren, New Jersey). Covered stents were manufactured in the catheterization laboratory under sterile technique, using ultrathin ePTFE tubing 10 cm x 8 mm (Zeus, Orangeburg, South Carolina) cut to appropriate length to cover the metal stent exterior (Figures 1 and 2) as previously reported [11].

We altered the method later in our practice by abandoning the suturing technique and instead front-loading the stent prior to application of the covering. The covered stent was then crimped onto the balloon, which had already been threaded through the sheath and tucked back slightly until slightly covered by the sheath. In this latter method of front-loading the stent, we were able to minimize the traction and shear force on the ePTFE covering

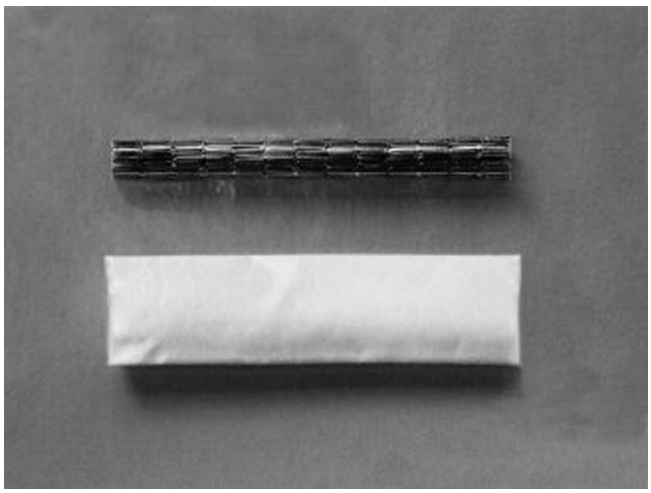

Figure 1. Image demonstrating the bare metal stent and ePTFE cut to an appropriate length to cover the stent.

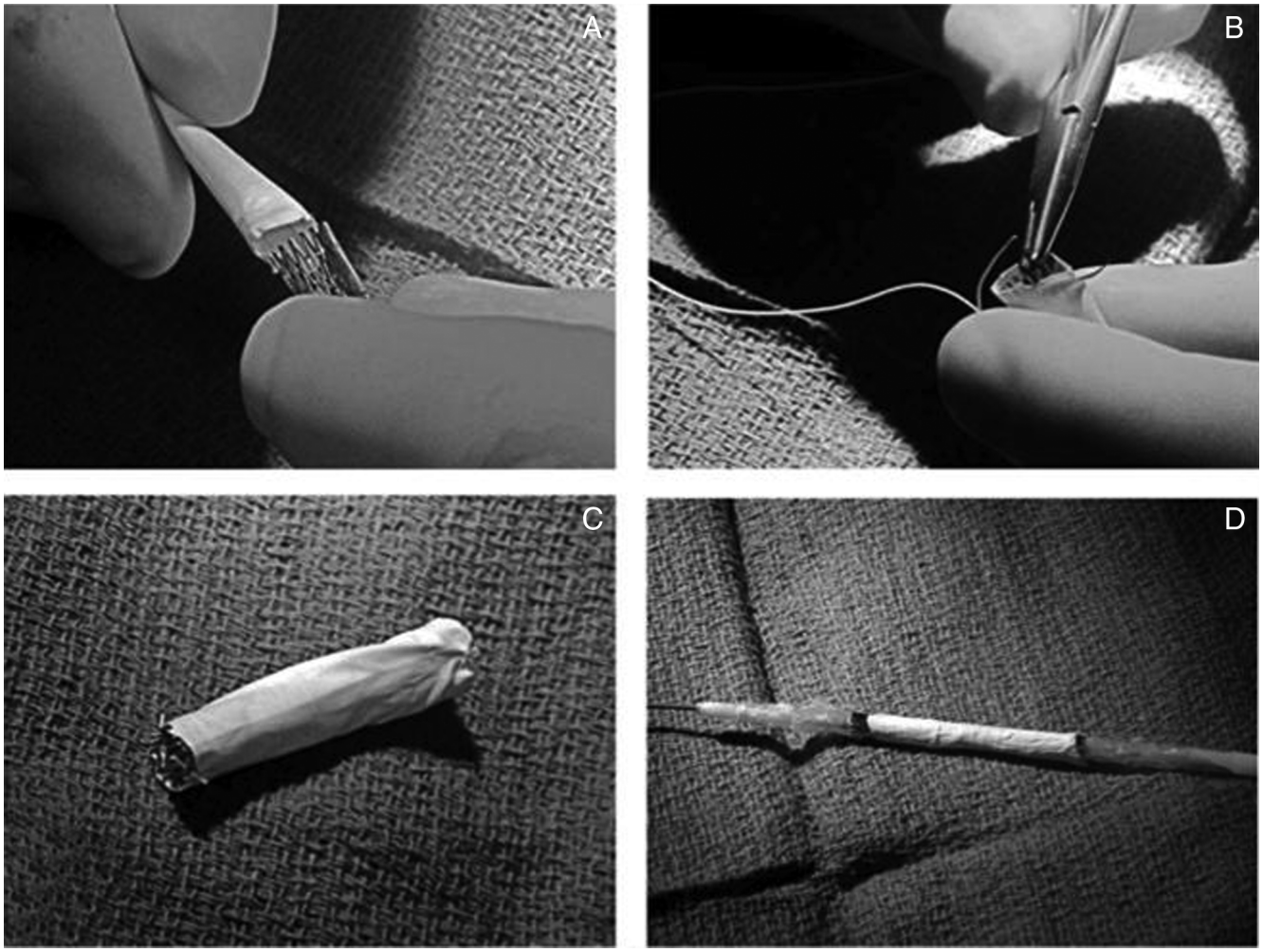

Figure 2. Series of images demonstrating (*Panel A*) application of the covering over the stent, (*Panel B*) suturing of the PTFE covering to the stent, (*Panel C*) the newly self-fabricated covered stent, and (*Panel D*) following crimping onto the balloon.

during deployment by reducing the distance of stent travel as per the initial method.

Procedure

All procedures were performed under general anesthesia in a dedicated cardiac catheterization laboratory and guided by biplane fluoroscopy. Patients received an initial bolus of intravenous heparin and antibiotics during the procedure. Femoral vascular approach was used in all cases. In two patients with aortic atresia, simultaneous brachial arterial approach was used to facilitate crossing the stenotic territory from below. Right internal jugular venous access was used in the case of the baffle leak for positioning across the stenotic lesion.

For the coarctation cohort, intravascular ultrasound was used pre- and post-stenting to assess internal dimensions and effects of stenting on vascular wall. Rapid right ventricular pacing was used to reduce the systolic blood pressure by at least 50% in appropriate cases. Following stent implantation, hemostasis was achieved with the aid of Perclose devices (Abbott Vascular Laboratories, Illinois) in thirteen patients. For the remainder of cases when the artery was felt to be too small, hemostasis was achieved with manual compression. Aspirin was administered to all patients post-procedure and continued at a dose of 5 mg/kg or maximum 325 mg daily for up to 6 months. Follow up included CT imaging and/or transthoracic echocardiography at 6 months.

Results

We implanted a total of 25 fabricated covered stents in 21 patients (12 male): (a) 17 patients with CoA (mean weight, 70.4 kg), (b) 3 patients with PA or RV-PA stenosis (mean weight, 48.3 kg), and (c)

Table 1: CoA Patient Demographics and Procedural Details

Pt	Sex	Age (yrs)	Wt (kg)	Pre-gradient (mm Hg)	Pre-dim (mm)	Stent	Post-grad (mm Hg)	Post-dim (mm)	Complications
1	F	24.0	61.0	33	0	MAX-LD 36	3	14	Aneurysm
2	M	14.7	67.4	-	-	PG3910	-	-	None
3	F	10.2	28.0	47	7	PG2910	17	11	None
4	M	42.4	80.5	40	2	PG2910	19	10	None
5	F	23.2	83.0	12	-	PG3910	0	-	None
6	F	29.9	59.1	20	5	MAX-LD 36	4	11.8	Fem thrombus
7	F	29.5	88.0	69	8	PG3910	8	14	None
8	M	26.5	48.5	35	0	PG3910	0	12	None
9	M	25.4	65.5	32	7.7	P4010	2	16	None
10	F	35.5	168	30	6.7	MAX-LD 36	7	16	None
11	M	35.0	80.5	20	13	MAX-LD 36	0	22	None
12	M	20.0	49.7	23	10	MAX-LD 36	0	16	None
13	M	8.9	36.2	53	3	MAX-LD 26	3	10	None
14	M	25.4	101.2	78	3.5	MAX-LD 36	17	10.5	None
15	F	25.8	135.4	8	12.5	P4010	2	20	None
16	M	48.6	70.3	40	-	MAX-LD 36	9	-	None
17	M	34.9	97.0	28	3.2	P4010	0	10.6	None

1 patient with a right-to-left shunt from baffle leak (weight 77.9 kg). The mean age at stent implantation for each group was 27.1, 24.7, and 25.1 years, with mean follow up 36, 8, and 17 months, respectively.

Group (a): Coarctation of the Aorta

Among patients with CoA, 12 had native coarctation, 4 had aneurysm formation following a previous intervention, and 1 had re-coarctation following surgery in infancy. Thirteen patients with native or re-coarctation had pre-procedural hypertension. Table 1 lists patient demographics.

The mean systolic pressure gradient fell from 35.5 mm Hg to 5.7 mm Hg (median change 32.5 mm Hg to 3 mm Hg; $p < 0.001$) following stent implantation (Figure 3). The mean diameter of the CoA increased from 5.83 mm to 13.9 mm (median increase 5.85 mm to 13 mm; $p < 0.001$) post-procedure. There was no residual leak seen on angiography immediately following stent deployment in those patients

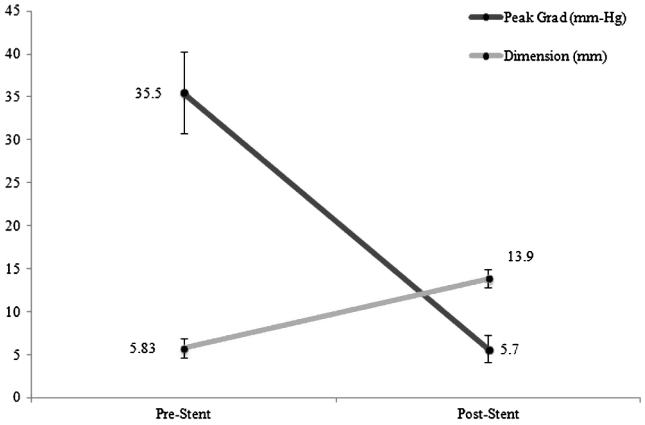

Figure 3. Changes in peak systolic gradient and aortic dimension pre- and post-stent for patients with CoA.

with previous aneurysm formation. Median femoral arterial sheath size was 12-Fr (range, 11- to 14-Fr).

One procedure was complicated by femoral artery thrombosis and required femoral thrombectomy. This patient was 30 years old and 59 kg at the time of the procedure and required a 13-Fr sheath for stent deployment. She recovered completely with no sub-

sequent complications. Another patient developed aneurysm following stent deployment. This patient was 24 years old with a severe coarctation with a gradient of 33 mm Hg across the stenotic lesion. A self-designed 36 mm long MAX-LD (ev3) covered stent mounted on a 16 mm Z-MED balloon (NuMED) was deployed. Immediately after stent deployment, repeat angiogram revealed the presence of a contained dissection. A 3.4-cm-long, 22 mm-diameter self-expanding stent graft (Medtronic, Minneapolis, Minnesota) was implanted during the procedure with exclusion of flow into the aneurysm. Because of the profile (diameter and length) of the delivery system, a cut down to the left iliac artery was performed to compensate.

Mean follow up was 36 months (range, 1–83 months). Eleven patients had routine follow-up CT scan performed at 6 months post-procedure with no evidence of new aneurysm or flow into residual aneurysm. Four patients underwent planned repeat stent dilatations between six and eight months after implantation. Mean clinic systolic blood pressure was reduced from 149 mm Hg to (95% CI: 128–161 mm Hg) pre-procedure to 125 mm Hg (95% CI: 114–135 mm Hg) following procedure ($p < 0.001$).

Group (b): PA or RV-PA Stenosis

The three patients with PA or RV-PA stenosis presented with dyspnea on exertion. The first patient had left branch PA stenosis with an associated distal left PA aneurysm measuring 13 mm. The second had proximal right PA stenosis. The last patient had a prior Ross procedure with subsequent RV-PA homograft conduit placement. After 7 years, he developed elevated RV pressures (80% systemic) and systolic dysfunction due to severe conduit obstruction. He underwent pre-stenting of his RV-PA conduit with two self-fabricated covered stents followed by transcutaneous pulmonary valve replacement with an Edwards SAPIEN 26 mm valve (Edwards Lifesciences Corp., Irvine, California). Table 2 lists patient demographics.

The mean systolic pressure gradient across the stenotic lesion fell from 37.7 mm Hg to 8.7 mm Hg (median change 34 mm Hg to 8 mm Hg) following stenting (Figure 4). RV systolic pressure decreased from mean 59.3 mm Hg pre-stent (median 59 mm Hg; range, 38–81 mm Hg) to 34.3 mm Hg (median 34 mm Hg; range, 27–42 mm Hg). All procedures resulted in angiographic improvement with no residual stenosis and no complications.

Group (c): Right-to-Left Shunt from Residual Leak

The patient in group (c) was a 25 year old man weighing 79.9 kg who presented with baseline hypoxia (oxygen saturation 85%) and exercise-induced shortness of breath. He had a history of L-transposition of the great arteries status post Mustard/Rastelli repair. He presented with a superior baffle leak and right-to-left shunt from superior vena cava to the left atrium at the site of a prior anastomosis.

He underwent placement of an ePTFE-covered P4010 stent over a 20 mm BIB. After stent deployment and upon further inspection, a linear density on fluoroscopic imaging was seen superior to the stent with persistent narrowing inside the stent. The density was attributed either to soft tissue from a prior procedure (pacemaker lead extraction on the day prior to stenting) or inversion of the ePTFE cover-

Table 2: PA and RV-PA conduit stenosis patient demographics and procedural details.

Pt	Sex	Age (yrs)	Wt (kg)	Lesion location	Pre-gradient (mm Hg)	RV pressure pre-stent (mm Hg)	Stent	Post-gradient (mm Hg)	RV pressure post-stent (mm Hg)	Complications
1	F	8.9	22.8	Left branch PA with aneurysm	34	59/10	MEGA LD 36	8	27/8	None
2	F	44.1	58.5	Proximal right PA	21	38/12	MEGA LD 36	0	34/10	None
3	M	22.6	63.5	RV-PA conduit	58	81/16	P4010, P4010	18	42/12	None

PA = Pulmonary Artery; RV = Right Ventricle

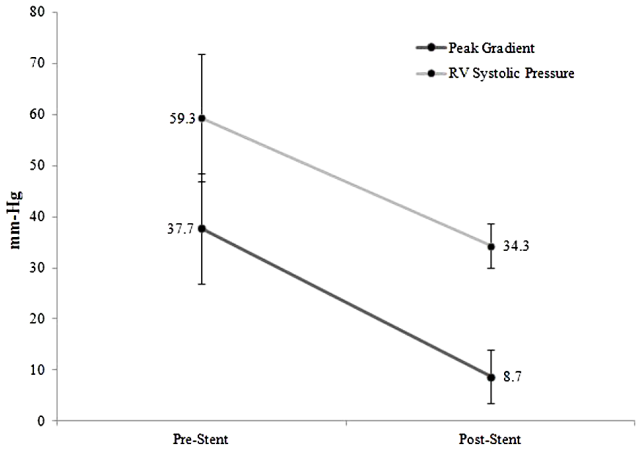

Figure 4. Reductions in peak systolic gradient and RV systolic pressure following stenting of pulmonary artery or right ventricle-to-pulmonary artery conduit stenosis.

ing. A self-expanding Gore Excluder was implanted in the previously placed stent with good stent apposition and no evidence of narrowing or residual leak from the superior aspect of the baffle. At follow up, oxygen saturation on room air had improved from 85% pre-intervention to 96% post-stent and he had significant improvement in symptoms.

Discussion

The complexity of transcatheter interventions in congenital heart disease will need to evolve to keep up with an aging population of CHD who have previously had palliative surgeries. The use of covered stents will expand the options available to adult patients, especially in high-risk cases where surgery may not be a feasible option [12].

In patients with CoA, the risk for late-term aneurysm formation with bare metal stent is 4–7% [13-15]. In patients with PA stenosis, the restenosis rate with angioplasty alone approaches 15% with a 4% risk of aneurysm [16-18]. Perhaps more importantly, current data estimates the risk of conduit rupture or trauma during transcatheter pulmonary valve replacement at 6% [19]. Late baffle leaks in patients with a history of Mustard or atrial switch is high as well, occurring in up to 25% of patients with these prior surgeries [20]. The numbers reflect a glaring demand for improved covered percutaneous therapies for adults with CHD.

In this study, we describe our innovative method of designing a covered stent using "on-the-shelf" materials that are already readily available, specifically applying ePTFE to a bare metal stent. The main indication of covered stent in groups (a) and (b) was acute or pre-existing aneurysm, or concerns regarding potential for vessel or conduit rupture due to severe stenosis or calcification. Patients deemed higher risk were generally older individuals in circumstances where stenotic thinning and reduced vessel wall compliance predisposed to dissection, rupture, or even death [3, 21]. The delivery sheath was 2- to 3-Fr larger than the recommended size for the balloon to accommodate the stent, as is consistent with the recommendations for delivery of the CP stent (NuMED, Inc.) [22].

Our preliminary results in the wider spectrum patients warranting stent intervention described here are excellent. In group (a), the median reduction in systolic pressure gradient from 32.5 mm Hg to 3 mm Hg is comparable to other cohort studies of patients treated with the CP or Advanta V 12 stent [2, 5, 6, 19, 23]. Only one patient developed contained aortic dissection treated effectively with self-expanding stent graft, highlighting that dissection and extravasation may still occur with balloon-expandable covered stents [16, 17, 21].

Additionally, group (b) demonstrated significant improvement in both stenotic gradient and RV pressure changes following RVOT stenting. In group (b), one patient had placement of an ePTFE-covered stent as a pre-stent for pulmonary valve replacement, elaborating the potential utility for covered stents in this population. Group (c) was limited to one patient but demonstrated elimination of right-to-left shunt after covered stent, although there may have been inversion of the covering which required a self-expanding Gore Excluder. Our results demonstrate safety and efficacy of our large diameter self-fabricated stent with effective reduction in stenotic gradients, and open the door for expanded application in patients with right-to-left shunts from late baffle leaks.

The covered CP stent was first approved in the United Kingdom in 2004, and the high demand is reflected in large number of stents being shipped from NuMED to European nations (personal communication, NuMED, Inc.). Given that the covered stent has been in widespread use for over a decade in

Europe, the delay in approval from the FDA is alarming, especially since ACHD are being treated every day across the country but the covered CP stent is only available in highly select centers in the United States under compassionate and emergency use.

Since the publication of our last article first describing our innovative and historic technique of designing covered stents [11], we received numerous inquiries into where we sourced the ePTFE, our methodology, and how we should be utilizing these stents, again echoing the great need for these stents by other providers. Since our publication, Zeus Inc. has unfortunately discontinued availability of the ePTFE covering for this recommendation due to concerns over how it was being used. Nonetheless, our results here demonstrate the technical feasibility of fashioning the covered stent. Although there were initial concerns regarding slippage of the covering created by traction of the stent through the sheath, we have been able to mitigate this issue by front-loading the stent into the sheath after the balloon is threaded first.

We acknowledge that our method of stent production is not an ideal solution, nor should it be overused or abused. Indeed a recent randomized controlled trial comparing bare and covered stent implantation for the treatment of severe native coarctation in adults did not demonstrate any benefit in using a covered stent [24]. However, aortic wall injury will occur and the availability of a covered stent is a necessity to any endovascular intervention where a vessel narrowing is being stretched. Although the covered stent is available for coronary and peripheral interventionalists, the notion that we must create our own covered stents for adults with CHD to provide a safe therapeutic option is an injustice to this population of patients. As a collective group, we are providing a disservice to our patients by not having these stents readily available, especially since they are already in widespread use in other parts of the world. The FDA's allowance of their use in the U.S. under compassionate or emergency use in select centers is in reality a consolation for the underlying failure to ensure that patients have adequate accessibility to what should be considered standard basic and safe care.

Three clinical trials (COAST II, PARCS, and Advanta V12 Atrium covered stent for CoA) are already underway looking at the use of covered stents in congenital heart disease. Of these trials, only PARCS is examining the role of covered stents for PA repairs and has already yielded early results on safety and efficacy [19]. Still, the CP and Advanta stents are many years away before being commercially available in standard catheterization laboratories and our need for covered stents to provide proper care is now.

Our need for covered stents will continue to grow. As transcatheter pulmonary valve implantation evolves at a faster rate, there is growing concern over vessel rupture or trauma, especially with the 4–6% risk of conduit disruption and the risks of expanding homografts already reported [17-19]. These risks are not unreal, and we need a stent to protect against these complications as part of basic care.

Covered stents increase the interventionalist's options for treating high-risk stenoses, aneurysm or baffle leak in adults with CHD. In this study, we show successful reduction in gradients after implantation of self-fabricated covered stents. Additionally, we examine the promising extended application of these stents in adults with branch pulmonary stenoses and baffle leaks with excellent preliminary results and symptom relief. Our study sheds light onto the innovative interventional strategies that can be used to treat the expanding and challenging population of ACHD.

Conflict of Interest

Ziyad M. Hijazi is a consultant to NuMed, Inc.

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Cite this article as: Wadia SK, Kenny D, Alkashkari W, Matella T, Kavinsky CJ, Hijazi ZM. Extended Application of Self-Fabricated Covered Stents for Interventions in Adults with Congenital Heart Disease. Structural Heart Disease. 2016;2(3):79-86. DOI: http://dx.doi.org/10.12945/j.jshd.2016.003.15

D7 / COMPLICATION WHILE STENTING OF LONG SEGMENTAL COA IN PATIENT WITH GOLDENHAR SYNDROME

D8 / TRANSCATHETER CORRECTION OF SCIMITAR SYNDROME; OCCLUSION OF ABNORMAL PULMONARY VENOUS DRAINAGE AND VASCULAR SUPPLY

D9 / SUCCESSFUL REPOSITIONING OF A MIGRATED DUCTAL STENT

E1 / LEFT VENTRICULAR ASSIST DEVICE OUTFLOW KINKS: A COMPLICATION OF SURGICAL PLACEMENT THAT COULD BE MANAGED BY PERCUTANEOUS STENTING

E2 / THE EVALUATION OF DIAGNOSTIC AND INTERVENTIONAL CARDIAC CATHETERIZATION PROCEDURES OF PATIENTS UNDER EXTRACORPOREAL MEMBRANE OXYGENATION SUPPORT

E3 / A COMPARISON OF CLINICAL OUTCOME BETWEEN SURGICAL REPAIR AND TRANSCATHETER OCCLUSION OF CONGENITAL CORONARY ARTERY FISTULA

E4 / TRANSCATHETER TREATMENT OF "COMPLEX" MALFUNCTIONING TRICUSPID VALVE PROSTHESIS AFTER SURGICAL REPAIR OF EBSTEIN ANOMALY

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E6 / NOVEL HYBRID APPROACH FOR MAPCAS ESTABLISHING FROM INTRAOPERATIVE DIRECT ANGIOGRAPHY OF DIMINUTIVE CENTRAL PULMONARY ARTERY CANNULATION

E7 / AORTIC RING AUTOGRAFT FOR RECONSTRUCTION OF THE NEO-PULMONARY ROOT IN THE ARTERIAL SWITCH OPERATION

E8 / DECREASING RADIATION EXPOSURE IN A PEDIATRIC INTERVENTIONAL ELECTROPHYSIOLOGY LABORATORY

E9 / SIMULTANEOUS MULTI-SITE THREE DIMENSIONAL ROTATIONAL ANGIOGRAPHY REDUCES CONTRAST AND RADIATION DOSE IN PATIENTS AFTER TOTAL CAVO-PULMONARY CONNECTION UNDERGOING CATHETERIZATION

E10 / STENTING OF SUBATRETIC COARCTATION OF AORTA GUIDED BY THREE DIMENSIONAL ROADMAP BASED ON COMPUTED TOMOGRAPHY OR MAGNETIC RESONANCE IMAGING DATASETS

E11 / DETAILED ECHOCARDIOGRAPHY IS CRUCIAL FOR TRANSCATHETER PARAVALVULAR LEAK OCCLUSION; SPONTANEOUS GRADUAL RESOLUTION OF MASSIVE HAEMOLYSIS AFTER OCCLUSION

ANTITHROMBOTIC TREATMENT AFTER PERCUTANEOUS LEFT ATRIAL APPENDAGE CLOSURE: A DIFFICULT CHALLENGE IN PATIENTS AT HIGH RISK OF BLEEDING

Daniele Gemma [1], Guillermo Galeote García [1], Raúl Moreno Gómez [1], Javier De Juan Bagudá [2], Natalia Lorenzo Muñoz [3], Ignacio Plaza Pérez [2], Inés Ponz de Antonio [1], José Luis López Sendón [1]

1. Hospital Universitario La Paz, Madrid, Spain
2. Hospital Infanta Sofía, Madrid, Spain
3. Hospital Infanta Cristina, Parla (Madrid), Spain

BACKGROUND: Contraindication to oral anticoagulation (OAC) is the main indication for percutaneous left atrial appendage closure (PLAAC). This implies a challenge in deciding the adequate antithrombotic therapy after device implantation.

OBJETIVE: The aim of our study is to assess whether the type of antithrombotic treatment is related to thromboembolic/bleeding risk after PLACC.

MATERIALS: Retrospective observational study including patients with atrial fibrillation who underwent PLAAC with AmplatzerTM device for OAC contraindication in our centre, until April 2015. Major bleeding was defined as intracranial bleeding, decrease in Hb ≥ 2 g/L and/or transfusion requirement, and minor bleeding as any other kind of bleeding.

RESULTS: 18 patients were included (mean age 75 years, HASBLED 4). After PLAAC, control transesophageal echocardiography was performed in 14 patients; 12 patients (66.6%) received dual antiplatelet therapy (DAPT), 3 (16.7%) single antiplatelet therapy (SAPT), 3 (16.7%) apixaban for 3 months. No device thrombosis was observed. Bleeding was observed in 5 cases (3 major, 2 minor), 4 of them in the first year, with an annual rate of major bleeding in the first year higher than expected by the HASBLED score (11.1% vs. 8.9%). 2 major bleedings occurred under DAPT, while the 2 minor bleedings occurred under SAPT. No bleeding was observed under apixaban. The only parameter associated with major bleeding was DAPT at discharge (p=0.001).

CONCLUSION: In our series DAPT after PLAAC was associated with a higher rate of bleeding complications. We didn´t observe device thrombosis. Further studies are needed to find the optimal antithrombotic regimen after implantation.

	Kind of bleeding	Age	Gender	HAS-BLED score	Time from intervention (months)	Antithrombotic treatment
Major bleeding	Esophageal varices (Exitus)	82	M	5	30	Nothing
	Intracranial (Exitus)	65	M	5	2	Acetylsalicylic acid 100 mg + Clopidogrel 75
	Intestinal (Transfusions)	74	M	4	1	Acetylsalicylic acid 100 mg + Clopidogrel 75
Minor bleeding	Haematuria	77	M	5	9	Acetylsalicylic acid 100 mg
	Epistaxis	93	F	3	6	Acetylsalicylic acid 100 mg

IMPORTANCE OF CARDIAC CT PRIOR TO A SECOND GENERATION TRANSCATHETER AORTIC VALVE IMPLANTATION

Ines Ponz, Daniele Gemma, Elena Refoyo, Emilio Cuesta, Guillermo Galeote, Zorba Blazquez, Juan Caro, Mar Moreno, Raul Moreno, Jose Luis Lopez Sendon

Hospital Universitario La Paz, Madrid, Spain

INTRODUCTION: The Lotus™ Valve (LV) is a second-generation transcatheter aortic prosthetic valve. Our aim was to identify predictors of potential complications related to its implantation.

METHODS: Prospective study including patients submitted to LV implantation between May 2014 and February 2015. Transthoracic and transesophageal echocardiography and Cardiac Computerized Tomography (CT) was performed before the procedure.

RESULTS: 16 patients underwent LV implantation: number 23 in 56.2%, 25 in 18.8% and 27 in 25% (62.5% female, mean age 80.5 years, mean EuroSCORE 9.65, Table1). After the procedure both mean and maximal gradient improved in all patients (p0.001), finding no predictors of such improvement.

We found a higher incidence of postprocedural complications among patients with a greater ascending aortic diameter by CT (37.9 vs. 32.6mm, p0.011), and with left ventricular dysfunction, particularly with renal failure (p0.001).

Pacemaker implantation (50%) was associated with a greater left ventricular outflow tract (LVOT) perimeter (73.6 vs. 65.2mm, p0.03) and calcification of the mitroaortic fibrosa (p0.001), which was also more frequent among patients developing bundel branch block (62.5%; p0.035).

12.5% suffered a cardiac arrest due to atrioventricular block, which was associated with a greater LVOT area (484 vs. 343mm2, p0.005) and perimeter (82 vs. 68.2mm, p0.002), measured by CT, and also with implantation of a bigger valve (p0.02).

CONCLUSIONS: Performing a Cardiac CT prior to a LV implant is useful to predict possible postprocedural complications. A greater LVOT with implantation of a bigger valve and the calcification of the mitroaortic fibrosa associate a greater risk of conduction disorders.

Table1: Echocardiographic or tomographic/radiographic characteristics

	Mean value
Valvular área (3D planimtry)	0,65 cm2
Pre-procedure maximal gradient	65,2 mmHg
Pre-procedure mean gradient	20,3 mmHg
LVEF	62,3%
Aortic annulus area (CT)	442,4 mm2
Aortic annulus perimeter (CT)	78,9 mm
Calcium Score	3048,6

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LOTUS, A NEW SECOND-GENERATION TRANSCATHETER AORTIC PROSTHETIC VALVE EFFICACY AND SAFETY

Daniele Gemma, Inés Ponz De Antonio, Raúl Moreno Gómez, Guillermo Galeote García, Elena Refoyo Salicio, José Luis López Sendón

Hospital Universitario La Paz, Madrid, Spain

BACKGROUND: Lotus™ Valve (LV) is a second-generation transcatheter aortic prosthetic valve (TAVI), retrievable and repositionable, designed to minimize the risk of complications, particularly periprosthetic aortic regurgitation (AR). Experience with this new TAVI is still limited.

OBJETIVE: The aim of our study is to report the results of our initial experience with LV implantation, in terms of safety and efficacy.

MATERIALS: Prospective study including patients with severe aortic stenosis who underwent LV implantation in our centre between May 2014 and February 2015. We report echocardiographic and clinical outcomes until hospital discharge.

RESULTS: 16 patients underwent LV implantation (62.5% female, mean age 80.5 years, mean EuroSCORE 9.65). During the procedure, a patient suffered a thrombotic occlusion of the left main coronary artery, which was corrected by thromboaspiration, without sequelae. No prosthesis embolization was observed. Following LV implantation, both mean and maximal gradient and AR improved in all patients (p0.001), with no cases of periprosthetic AR post TAVI. Pulmonary systolic pressure was reduced in 50% of patients (see Table). 8 patients suffered complete atrioventricular block until eight days after the procedure, requiring pacemaker implantation. The average hospital stay was 5 days, without any exitus at discharge.

CONCLUSION: Lotus is an effective and safe alternative for the treatment of patients with severe aortic stenosis and high surgical risk, despite a relatively high incidence of conduction disorders in our initial experience. Studies are needed to better patient selection for this type of TAVI.

	Pre-Lotus	*Post-Lotus*	*P*
Maximal Gradient	65,2 mmHg	20,2 mmHg	p 0,001
Mean Gradient	20,3 mmHg	10,1 mmHg	p 0,001
Aortic regurgitation	68,8% grade I or II	18% grade I	p 0,001
Pulmonary Artery Systolic Pressure	51 mmHg	39,9 mmHg	p 0,01