

On Topaz Cardiovascular Thrombus

From Pathology and Clinical Presentations to Imaging,
Pharmacotherapy and Interventions



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Cardiovascular Thrombus

From Pathology and Clinical Presentations to
Imaging, Pharmacotherapy and Interventions

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The Role of Interventional Cardiology in the Management of Thrombotic Conditions in the Pediatric Population

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INTRODUCTION

Children with complex disease requiring intravascular manipulation are at the greatest risk for thrombosis and thromboembolism. In 2009, Raffini et al. [1] described a 70% increase in the number of children hospitalized with venous thromboembolism (VTE) over a 7-year period across the United States. Early recognition and treatment decreases the likelihood of patient morbidities, including clot propagation, pulmonary embolus, and postthrombotic syndrome (PTS), as well as mortality [2].

Children possess several unique physiologic features of their clotting and fibrinolysis cascades, which affect not only their probability to form clots, but also their response to treatments and long-term outcomes. Systemic thrombolysis, though frequently used, has a narrow safety margin and carries a significant risk of bleeding in the pediatric patient. Surgical intervention has mixed results and is typically reserved for patients who have failed thrombolytic therapy or who are at high risk for complications with interventional therapy. Percutaneous treatment for thrombosis has emerged as an attractive and a less invasive alternative to surgical intervention. Transcatheter recanalization has been used with considerable success in patients with superior vena cava (SVC) syndrome, occluded systemic-to-pulmonary artery shunts, and occluded pulmonary arteries and in arterial and venous pathway obstruction.

ETIOLOGY OF THROMBOSIS

Coagulopathy in the patient can be explained based on Virchow's triad [3], which can occur because of alteration in the blood composition, flow abnormality, or change in the vessel integrity. Quantitative deficiencies and qualitative mutations can exist in virtually every protein in the coagulation cascade [4]. Inherited thrombophilia, coupled with an acquired risk factor, can place the patient at a risk for thrombosis. Acquired risk factors [5] are numerous and include the presence of a central venous catheter, immobilization following trauma, complex congenital heart disease, disseminated intravascular coagulation, and malignancy.

CONSEQUENCES OF THROMBOSIS

Complications associated with vessel thrombosis include chylothorax, chylopericardium (from high central venous pressure in the left subclavian vein), portal or pulmonary hypertension, SVC syndrome, catheter-related sepsis, and the long-term need for anticoagulation [6]. PTS [7,8] occurs in 65% of the children with VTE and is characterized by pain, swelling, visible collateral vein formation, and skin abnormalities at the site of a previous thrombus. It occurs because of venous hypertension, which develops secondary to obstruction or reversal of venous flow.

TRANSCATHETER THERAPY

Transcatheter therapy for the treatment of thrombosis [9] employs various techniques, including suction or aspiration thrombectomy, balloon dilation, stent placement, rheolytic thrombectomy, mechanical thrombectomy with fragmentation of the thrombus, and rotational thrombectomy. Mechanical and rotational thrombectomy have been sparingly used in the pediatric population and are typically reserved for use in patients with cerebrovascular accidents. The procedure selected for the pediatric patient varies based on the site of the occlusion and the presence of an organized or nonorganized thrombus. The equipment selected depends on the size of the patient, the segment being recanalized, and whether the thrombus is acute or chronic. In general, suction thrombectomy and rheolytic thrombectomy are much more effective in a nonorganized thrombus.

An MRI or computed tomography scan prior to the procedure is helpful in understanding the anatomy of the vessel segment, since the pathway is not always straight. Patients with hemodynamic instability such as in Blalock–Taussig (BT) shunt thrombosis can be placed on extracorporeal membranous oxygenation (ECMO) prior to the procedure. There are reports of intervention on a BT shunt through the side port of an ECMO cannula [10]. These procedures are relatively long and, therefore, general anesthesia is recommended. Biplane fluoroscopy is recommended since vessel reconstruction pathways may be complex.

SUCTION OR ASPIRATION THROMBECTOMY [11,12]

If the thrombus is recent and not organized, an attempt can be made to suction the thrombus. An aspiration catheter of varying internal diameter (0.044–0.072 in.) is advanced to the thrombosed segment and the distal end of the catheter is placed proximal to the clot. A negative pressure with a syringe is applied and the clot is suctioned into the catheter. Aspiration of the blood into the syringe providing suction indicates that the clot has been aspirated. The suction catheter may be advanced to a new position where the suction process can be repeated. If no blood return is obtained, it can be assumed that the suctioned thrombus is totally occluding the distal tip of the catheter and could be protruding from the catheter tip. In this situation, suction to the side port of the sheath with a syringe will allow aspiration of those clots that could shear off the tip of the suction catheter.

BALLOON ANGIOPLASTY AND STENT PLACEMENT

In patients in whom the thrombus is organized it is necessary to first perforate the thrombus and then balloon dilate and stent the vessel segment. The anatomy of the vessel to be recanalized should be defined, including the two ends of the occluded vessel, prior to perforating the thrombosed vessel segment. This can be accomplished by obtaining angiograms proximal and distal to the occlusion, such as in the iliofemoral vessels, the SVC, and in the baffle limbs following the Mustard/Senning repair. In many patients a dimple is noted at the site of the thrombus, which can be engaged with a catheter. The thrombus can be perforated with a wire, a transseptal needle, or the Nykanen radio-frequency (RF) ablation catheter. It is recommended that a long sheath be advanced to the thrombus, which would allow for catheter stability, contrast injection, and easy catheter exchanges. Once the anatomy of the vessel and the target sites have been identified a catheter is engaged with the thrombus and a wire is advanced through the affected vessel segment. In patients with acute occlusion a hydrophilic coated wire will advance easily through the thrombus. In patients with chronic occlusion there is organization and tissue growth in the occluded vessel. Three-dimensional microcomputed tomography [13] has demonstrated that even in chronically occluded vessels there are multiple microchannels around the occluded vessel and, therefore, advancing a hydrophilic wire may be a possibility. There is a certain degree of force required to traverse an occluded segment, and using a straight path as opposed to an angle allows for optimal force to be applied (Fig. 40.1) [14] and decreases the chance of the wire going outside the vascular segment. Organized clots maybe difficult to cross, and a transseptal needle, the stiff end of a guidewire, or an RF catheter can be utilized to cross the lesion. When the occluded segment is difficult to cross it is important that the perforating wire be advanced slowly with firm pressure and that frequent hand injections be done to confirm an intraluminal course.

RF ablation [15,16] has been commonly used to perforate the pulmonary valve in patients with pulmonary atresia and intact ventricular septum. RF perforation can also be used to create a channel through the thrombosed vascular segments. A 4-Fr right Judkins catheter is used to maintain stable position against the occluded vessel and to determine the direction in which the RF wire will be advanced. A 0.016-in. Nykanen RF perforation wire is advanced through the guide catheter until resistance in the occluded vessel is felt. The Baylis RF generator and wire (Baylis Medical Company, Montreal, QC, Canada) are used to deliver serial RF bursts (10 W for 5–10 s) and the wire is progressively advanced under fluoroscopic guidance

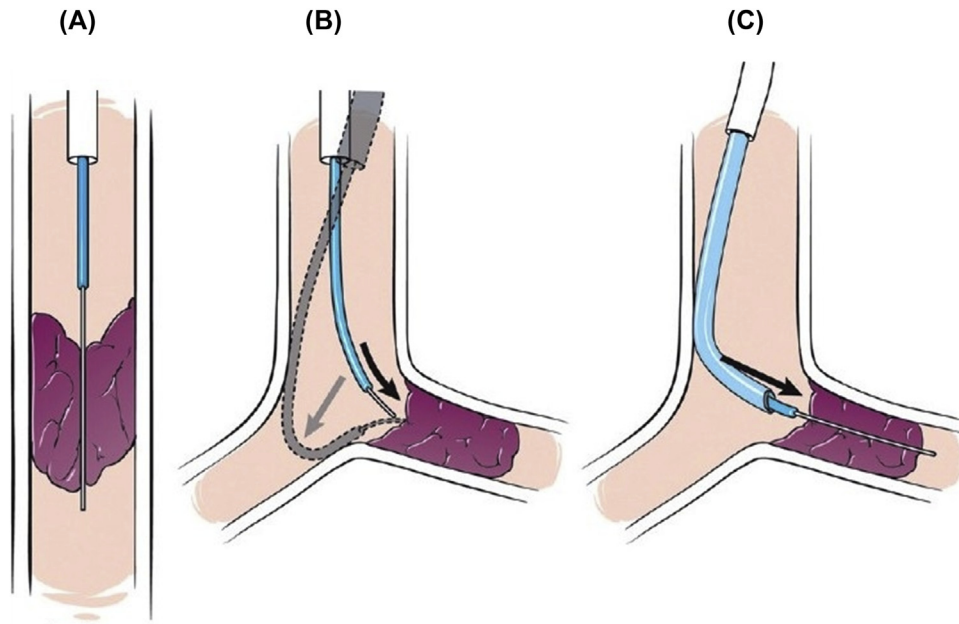


FIGURE 40.1 This series of diagrams illustrates the principles involved in optimizing the approach of a penetrating guidewire across vascular occlusions. A straight approach allows for the most penetrating pressure at the tip of the guidewire (A). If the occluded vessel comes off at a relatively sharp angle (i.e., the “neo” left pulmonary artery in a Glenn shunt), attempts to apply force with a guidewire through a catheter will result in the catheter being pushed away (B). This results in minimal force at the tip of the guidewire. The addition of a coaxial system (C) allows for a supporting catheter (i.e., guide catheter) to be buttressed against the vessel wall, in a stable position. This facilitates the application of enough force at the guidewire tip to cross the occluded segment. *Adapted from Latson L, Qureshi A. Techniques for transcatheter recanalization of completely occluded vessels and pathways in patients with congenital heart disease. Ann Pediatr Cardiol 2010;3:140–6.*

with frequent contrast injected by hand. A coaxial catheter (Baylis Medical coaxial injectable catheter) is advanced over the 0.016-in. wire. Through this catheter a stiffer wire is positioned and the balloon angioplasty catheter advanced.

After the thrombosed segment has been traversed with a guidewire, transseptal needle, or RF wire it is important to ensure that the tip is intravascular. This can be achieved with an angiogram obtained through the catheter. In addition, after the thrombosed segment has been crossed, a guidewire that moves freely in the vessel lumen helps confirm an intravascular position of the wire. If the distal tip of the wire can be snared, then a large catheter can be advanced over the wire; otherwise, a hydrophilic wire and catheter can be advanced. With a passage created across the thrombosed vessel a low-profile balloon catheter is inflated to dilate the tract. To create an adequate-sized lumen, a high-pressure balloon can be inflated across the thrombosed segment or an intravascular stent can be placed. Following the procedure anticoagulation and antiplatelet therapy is continued for 2–3 months. Long-term patency of the stents in thrombosed vessel segments has not been reliably documented. Should thrombosis of the stent occur or there is a need to redilate the stent further as the child grows, the vessel segment can be reaccessed and the stent dilated.

There are few reports of complications from attempted transcatheter recanalization of vessels. Should a perforation occur it is recommended that the balloon be advanced across the area to occlude the vessel and a covered stent be placed over the site of perforation.

THROMBOSIS IN CONGENITAL HEART DISEASE

The incidence of thrombosis and thromboembolism is the highest in children with congenital heart disease for a multitude of reasons [17]. Patients with congenital heart disease have abnormalities in coagulation proteins [18] coupled with contributing risk factors such as surgical procedures, central venous line placement, hemodynamic instability, and repeat cardiac catheterization. Patients with single ventricles, systemic-to-pulmonary artery shunts, and prosthetic valves are at a risk of thrombosis and thromboembolism [19–21].

Children with cardiac disease often have an imbalance in hemostasis predisposing them to thrombosis, paradoxical bleeding, or both. In children with congenital heart disease [22–26] there are abnormalities in coagulation proteins (factors II, V, VII, IX, X), fibrinogen is decreased, factor VIII is increased, inhibitors of coagulation proteins C and S are

decreased, and fibrinolytic proteins are decreased. Nowak-Gottl et al. [26] reported that increased levels of plasminogen activator inhibitor-1 in patients with congenital heart disease cause a decrease in fibrinolysis. The etiology of the alteration in the coagulation proteins is not known, since the hepatic synthetic ability is known to be normal in these children. The hemostatic abnormalities are seen in both cyanotic and acyanotic heart disease. In cyanotic heart disease it is hypothesized that cyanosis, low cardiac output, or a genetic predisposition may be the contributing etiologies. In acyanotic heart disease there is normalization of the quantity of factors by 5 years of age [22,25].

CARDIAC SURGERY

Cardiac surgery affects two arms of Virchow's triad via changes in blood flow and endothelial damage. In any cardiovascular procedure, endothelial damage results from even the smallest and most delicate intravascular sutures and manipulations. Blood flow can be altered in many ways secondary to cardiac surgery, from small diversions in blood flow as in the BT shunt to large alterations such as the Fontan circulation. Patients with BT shunt can have pulmonary artery stenosis at the site of shunt insertion, further exacerbating the risk of thrombus. Following the Fontan procedure, patients have an increased tendency to sustain a VTE event, with the incidence ranging from 3% to 16% [27]. Any setting for right-to-left shunting (like patent foramen ovale or atrial septal defect) creates a predisposition for strokes by creating a direct pathway between the venous and the cerebral arterial circulation in patients with VTE [28].

SYSTEMIC-TO-PULMONARY ARTERY SHUNT THROMBOSIS

In patients with cyanotic congenital heart disease, a systemic-to-pulmonary artery shunt such as a modified BT shunt or a central shunt [29] will increase pulmonary blood flow prior to a definitive repair. In a modified BT shunt a Gore-Tex tube graft is placed between the subclavian artery and the ipsilateral pulmonary artery, and in the central shunt a Gore-Tex tube of a known diameter is placed between the ascending aorta and the pulmonary artery. The Gore-Tex tube ranges from 3 to 4 mm in diameter depending on the size of the infant. The thrombosis of these small-caliber tubes can occur acutely or chronically, resulting in compromised pulmonary blood flow and hypoxemia. The risk of shunt thrombosis [19,20], which can be life threatening, ranges from 8% to 12%. Catheter-based interventions [29–32] in this subgroup of patients are emergent and lifesaving. In acute BT shunt thrombosis the treatment is thrombolytic therapy followed by balloon angioplasty or stenting of the shunt. Factors that lead to thrombosis are a kink in the shunt, stenosis at the anastomotic pulmonary or aortic site, antegrade flow across the pulmonary valve and competitive flow from the patent ductus arteriosus, aorta-to-pulmonary artery collaterals, or another shunt. Dehydration and hemodynamic instability also contribute to shunt thrombosis.

Recanalization of the shunt is demonstrated in Fig. 40.2. A 4-Fr sheath is placed in the femoral artery. The shunt is accessed with a 0.014-inch coronary guidewire through a 4-Fr Judkins right catheter. A long sheath is advanced to the mouth of the shunt. A premounted coronary artery stent sized to the diameter of the shunt is advanced across the shunt and delivered. The position of the stent prior to and following placement is confirmed through the side port of the sheath.

Petit et al. [29] reported the placement of stents in eight patients with a modified BT shunt, with a median weight of 4.4 kg (1.8–9 kg) and a median age of 55 days (7–410 days). In five of the eight patients shunt thrombosis was the indication for intervention. In one patient the stent could not be placed because of acute angulation of the shunt. Procedural success occurred in all patients. In one patient there was repeat thrombosis at 6 days and another stent was placed. This procedure has been reported to have been done safely in first postoperative week [30].

The most common subgroup of pediatric patients treated with balloon angioplasty or vessel stenting includes patients with single ventricular palliation. A study based on 20 years of experience with transcatheter interventions for treatment of obstructed systemic-to-pulmonary shunt was published by Bonnet et al. [30]. There were 33 procedures in 28 patients performed at a median age of 0.6 years and a median weight of 5.8 kg. There were 33 balloon angioplasties and 14 stent placements. The study demonstrated a long-lasting success rate of close to 78% following transcatheter interventions. The incidence of major procedural complications was noted to be 9% and there were no procedural deaths. The authors concluded that transcatheter therapy can be considered an efficient rescue strategy to restore patency of a thrombotic shunt.

VESSEL REHABILITATION

Vessel thrombosis can occur following vessel access for cardiac catheterization and line placement for infusions and monitoring in the critically ill young. The loss of vascular access in a patient dependent on dialysis or parental nutrition can

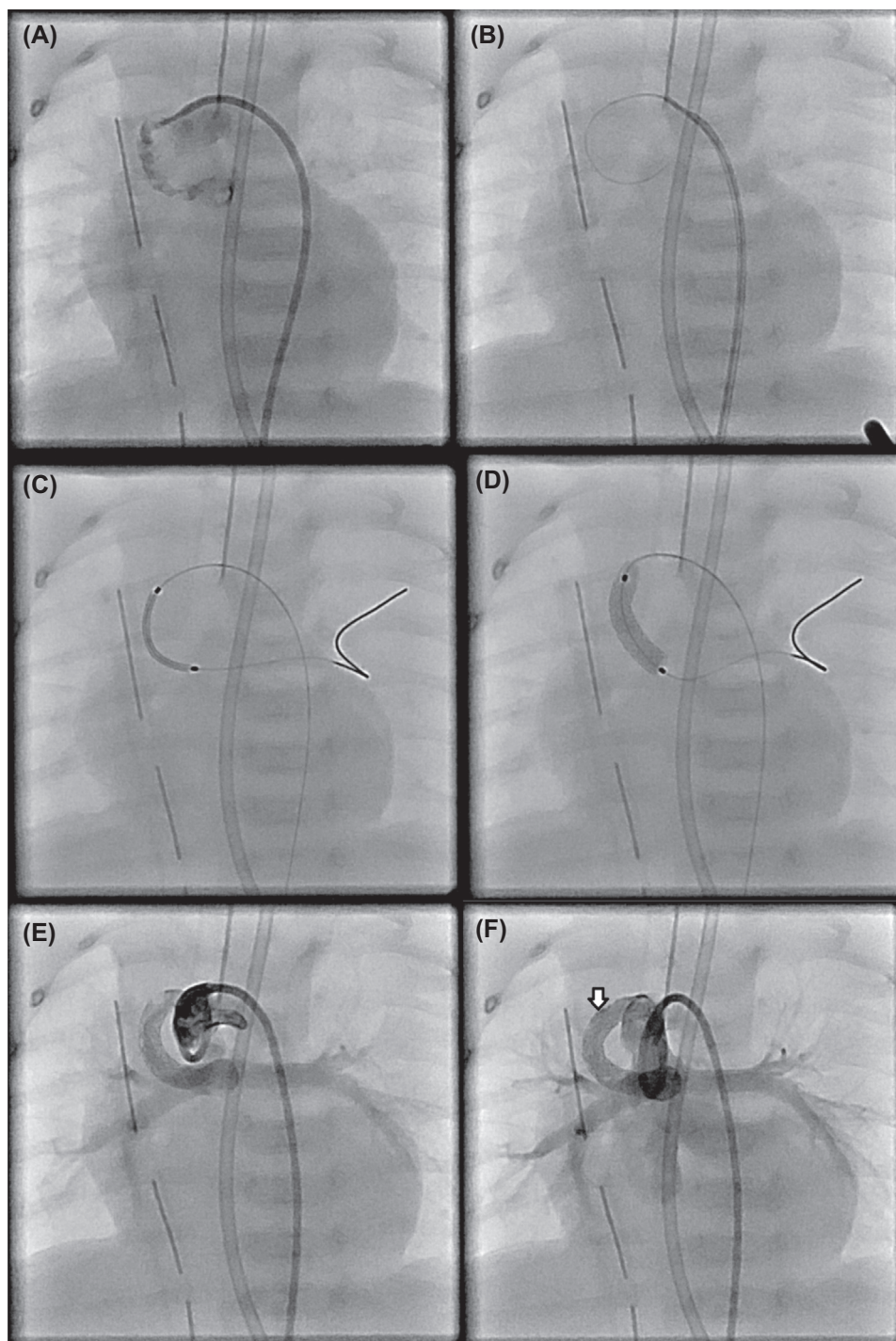


FIGURE 40.2 (A) Angiogram demonstrating occlusion of the central shunt with a thrombus. (B) A 0.018-inch hydrophilic wire in the pulmonary artery across the shunt. (C) A coronary artery stent over a wire across the thrombosed shunt. (D) Stent delivered across the shunt. (E) An angiogram following placement of the stent demonstrating a filling defect proximal to the stent. (F) A second overlapping stent is placed with a wide open shunt (arrow) demonstrating a filling defect proximal to the stent.

be life threatening. Thrombosis can preclude access to vessels, which is particularly important in patients with complex congenital heart disease in whom repeat catheterization may be needed.

There are multiple studies [33–35] that have identified younger age, smaller weight, and increased procedural time as the potential risk factors for increased incidence of thrombosis of the access site following cardiac catheterization

in pediatric patients. In addition, the ratio of the sheath size to the vessel size and the length of cannulation may contribute to thrombosis. In patients with arterial or venous thrombosis, percutaneous thrombectomy can be limb saving and should be considered as a treatment option. The incidence of deep venous thrombosis (DVT) following cardiac catheterization ranges from 0% to 27% [36–39]. PTS is a known complication of persistent or recurrent DVT. The incidence of arterial thrombosis with loss of pulse is reported to be between 8% and 39% in children weighing less than 14 kg despite the use of prophylactic heparin at the time of procedure [33]. Ding et al. [34] reported that the use of long sheaths and a weight less than 5 kg are associated with increased incidence of arterial thrombosis following cardiac catheterization. If not treated adequately or appropriately, it can lead to leg length discrepancy and difficulty with access during subsequent catheterization procedures. In select patients in whom thrombosis occurs reverse recanalization of the vessel and stent placement may be an option.

Acute Occlusion

Pulse loss after arterial cannulation not responding to thrombolysis is an indication for percutaneous transluminal angioplasty to restore flow to the affected limb. The contralateral femoral artery is entered and balloon angioplasty of the affected vessel done. This carries the risk of additional vascular injury and should be considered judiciously.

Peuster et al. [40] reported a case series of nine infants, mean age of 74 days, who underwent recanalization and balloon angioplasty of thrombosed arteries following a retrograde cardiac catheterization. A follow-up Doppler showed no residual stenosis in seven patients and mild residual narrowing in two patients.

Chronic Occlusion

The most common risk factor for thrombosis and thromboembolism is the presence of central venous catheters. About 50% of upper extremity VTEs in children occur secondary to central venous catheters [41]. The propensity to clot stems from a combination of altered blood flow or endothelial damage by the catheter and the infusions. A central venous line–induced thrombus in the upper extremity can lead to total occlusion of the vessel and place the patient at a risk for SVC syndrome. In the single-ventricle patients this would cause difficulty in the placement of a cavopulmonary artery anastomosis. Balloon dilation and stent placement followed by anticoagulation is an effective alternative to establish continuity. Transcatheter reconstruction of the vessels is effective in femoral and iliac veins and arteries, the inferior vena cava (IVC), the SVC (Fig. 40.3), and the innominate vein. Balloon angioplasty may create an effective lumen that does not stay patent and, therefore, stent placement should be considered to achieve a lumen that will have long-term patency. Ing et al. [42] placed 85 stents in 24 patients for reconstruction of the iliofemoral and IVC with a late patency rate of 87%.

THROMBOEMBOLISM

In single-ventricle morphology following the Glenn or Fontan palliation, venous thrombosis can lead to decreased cardiac output, pulmonary embolism, vena cava syndrome, and persistent pleural or pericardial effusions. In this subgroup of patients rheolytic mechanical thrombectomy can be lifesaving. The AngioJet (Boston Scientific) is available in sizes from 4 to 8 Fr, which allows it to be used in both central and peripheral arterial and venous interventions in the pediatric patient. In the rheolytic thrombectomy technique, also called hydrodynamic thrombectomy, a high-speed jet of saline is directed toward a thrombus at a speed of 300 mph in a retrograde fashion, creating a Bernoulli effect around the catheter tip. The sludge that is formed is suctioned via a suction port on the catheter. Fig. 40.4 demonstrates an embolus in the right pulmonary artery of a patient with Fontan palliation. The AngioJet was used to treat the thrombus, followed by anticoagulation with patency of the right pulmonary artery following the procedure.

In the majority of patients this procedure is followed by balloon dilation with or without stent placement. The incidence of embolic phenomenon, which is an inherent risk in thrombectomy, was only 1 in 21 in a small pediatric patient series [28]. In adults, the reported incidence of hypotension and bradycardia is close to 79% with the use of the AngioJet, which could be related to the release of adenosine due to lysis of red blood cells. However, it has since been shown that limiting the use of the AngioJet to less than 5 s at a time is associated with decreased incidence of these adverse events. Blood products should be available while using the rheolytic system as it involves aspiration of sludge that contains blood.

Fleming et al. [43] described their results with the AngioJet thrombectomy system in 10 patients with life- or limb-threatening thrombosis. The patients were a mean of 23 days status post–congenital heart surgery. The mean age of the patients was 74 days and the mean weight of the patients was 4.3 kg. Percutaneous thrombectomy of the pulmonary artery was performed in four patients, systemic veins in two patients, a surgical aortopulmonary shunt in two patients, and an iliac artery in one patient. Eight patients had balloon angioplasty after the thrombectomy and two patients had stent placed in addition to the angioplasty. All patients had improved flow across the thrombosed segment.

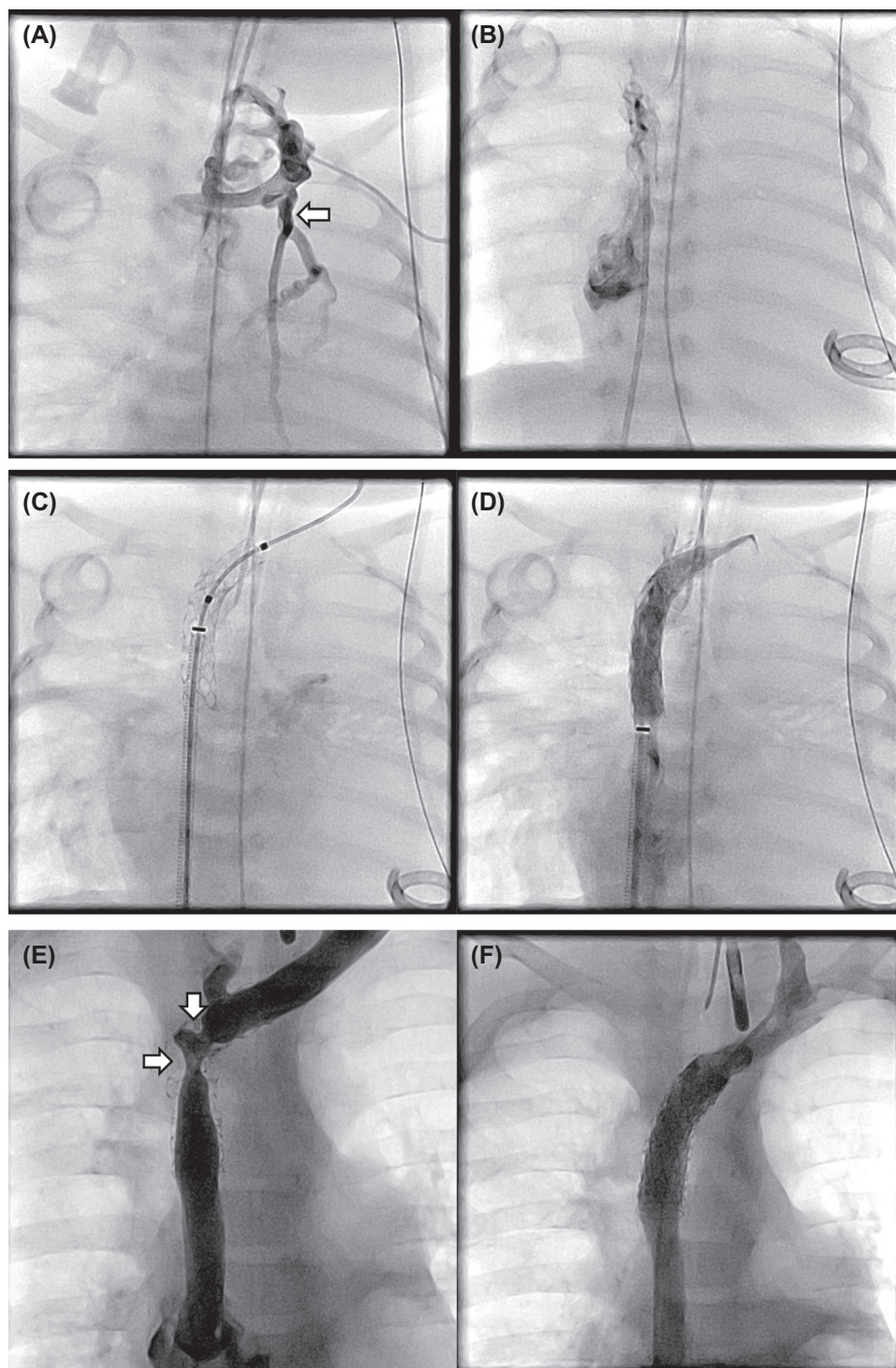


FIGURE 40.3 Patient with diaphragmatic hernia who was placed on extracorporeal membrane oxygenation with superior vena cava (SVC) syndrome. (A) Left innominate vein hand injection from a peripherally inserted central catheter line demonstrates complete obstruction of the innominate vein with multiple decompressing veins (*arrow*). (B) An SVC hand injection. (C) Two overlapping stents across the thrombosis. (D) An innominate vein injection demonstrates unobstructed flow from the innominate vein to the SVC. (E) An innominate vein hand injection 1 year later revealed a fracture of the stent and obstruction as indicated by *arrows*. (F) Innominate vein angiogram showing unobstructed flow from the innominate vein to the right atrium after placement of an additional stent across the narrowing.



FIGURE 40.4 Patient who is S/P Fontan with pulmonary artery obstruction from thromboembolism. (A) Superior vena cava (SVC) angiogram revealed no opacification of the right pulmonary artery (RPA) (*arrow*). (B) A lateral tunnel angiogram revealed opacification of the left pulmonary artery and SVC. The RPA is not opacified. (C) RPA angiogram done after AngioJet rheolytic thrombectomy showing wide open RPA.

VENOUS FILTER PLACEMENT

VTE is an underrecognized condition in the pediatric population. The placement of low-profile venous filters, mostly in the case of lower extremity DVT, is another modality of transcatheter intervention aimed at preventing distal embolization of thrombi. Venous filters are indicated in patients who cannot be anticoagulated or who have had breakthrough embolization on medical treatment. In addition, they are prophylactically placed in select patients with trauma. These are usually placed via femoral or internal jugular access through a 6- to 11-Fr sheath. Prior to placement of the filter, an angiogram is done to exclude any thrombus that could embolize during the procedure. The IVC filters are generally deployed below the level of renal veins to protect the renal vasculature. IVC filters are placed percutaneously and can be permanent or retrievable.

Biss et al. [44] reviewed 56 children with radiographically positive pulmonary embolism and stated that risk factors for thromboembolism were present in 54 patients (central venous line 35.7%, immobility 58.9%, recent surgery 28.6%). The most common underlying diagnosis was congenital heart disease in 28.5% of the patients. Reed et al. [45] reported placing the filters in eight children (six with contraindication to the use of heparin, one with idiopathic infrarenal IVC thrombosis, and anticoagulation in one). Raffini et al. [46] described the results of 11 filters placed in patients ranging from 6.8 to 23.4 years of age. There were nine retrievable filters and two permanent filters. In seven of the nine patients with retrievable filters, the filters were removed at a median of 37 days after placement. One patient died from malignancy. In the three patients with the IVC filter in place for 25–60 months, no patient had a subsequent pulmonary embolism. Rottenstreich et al. [47] described their experience of placing retrievable IVC filters in 59 patients with a low complication rate.

Data regarding safety and efficacy in the pediatric age group are lacking. Placement of a temporary or permanent IVC filter can be an important part of the treatment of IVC thrombosis in children.

COMPLICATIONS FOLLOWING CATHETER-BASED INTERVENTIONS

Complications of catheter-directed interventions for vascular thrombosis include perforation or dissection of the involved vessel, distal thrombus embolization, and death [44]. Other potential complications include chest pain, hemoptysis, blood loss, arrhythmias, contrast-induced nephropathy, anaphylactic reaction to iodine contrast, hemolysis (especially following the treatment of pulmonary embolism), and those known complications of vascular access, including hematoma, access-site thrombosis, arterial puncture, pseudoaneurysm, and arteriovenous fistula. In the case of a major complication, the procedure should be terminated as soon as hemodynamic stability is achieved, regardless of the angiographic result.

Fewer hemorrhagic complications should be seen with catheter-directed therapy than with systemic thrombolytic treatment, but no randomized control data trials have demonstrated this difference. However, the rate of major bleeding requiring blood transfusion with catheter-directed infusion of thrombolytic agents has been reported to be 46% [48]. The risks of minor and major procedural complications as defined by the Society of Interventional Radiology's clinical practice guidelines were 7.9% and 2.4%, respectively.

CONCLUSION

Thrombosis and thromboembolism are increasingly being recognized in children who are critically ill requiring intravascular manipulation. The treatment modality selected for treatment in the pediatric patient has to take into consideration the weight of the child, size of the vessel, and long-term patency of the vessel. Over the past 2–3 decades percutaneous transcatheter interventions have emerged as an attractive and efficient alternative to surgical intervention in the treatment of refractory thrombosis and thromboembolism. Thrombosed vessel segments can be reconstructed safely and effectively with satisfactory results. Long-term patency of these vessels has not been well documented at this time. Ongoing evaluation of treatment modalities is needed in this vulnerable and growing population.

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