ELSEVIER

Seminars in
ROENTGENOLOGY

# The Role of Interventional Radiology in the Treatment of Acute Thrombosis and Chronic Veno-Occlusive Disease in Children and Adolescents

Anne E. Gill, MD,* and Kavita N. Patel, MD†,‡

## Introduction

Pediatric venous thromboembolism (VTE) is an increasingly encountered entity in community and children's hospitals. Rates of pediatric VTE are reported to be rising and are approximately 0.07-1 in 10,000 children in the general population and 38-54 per 10,000 hospital admissions.[1-4] The age range for increased VTE risk in childhood is well established, with highest risk in infants (<1 year of age). Following infancy, the VTE risk decreases until adolescence when risk begins to rise and continues to rise throughout adulthood.[2,5,6] VTE provoking risks factors are usually present in children; the majority of whom have been reported to have at least 1 risk factor, with the most common being presence of a central line.[2,6,7]

Pediatric VTE has long- and short-term consequences. Treatment of VTE aims to ameliorate these complications. In the short term, management goals focus on limiting clot propagation/extension, decreasing the risk of embolization, preventing early VTE recurrence, and decreasing mortality. Pediatric VTE mortality risk is estimated to be approximately 2%, although in certain subgroups the risk may be higher.[8] With regards to long-term consequences, goals are often focused on prevention of VTE recurrence, decreasing risk of post-thrombotic syndrome (PTS), and maintaining vascular access and patency.[9]

Pediatric VTE encompasses many subtypes of thrombosis that have unique presentations, risk factors, and different considerations for management. Three subtypes will be discussed in this review: deep venous thrombosis (DVT) of the upper and lower extremities, pulmonary embolism (PE), and caval thrombosis (inferior vena cava [IVC] and superior vena cava [SVC]).

Approaches to the management of pediatric VTE may be standardized to some degree but often become personalized for individual children given the unique clinical presentation and medical history. Treatment strategies for pediatric VTE include anticoagulation, systemic thrombolysis, catheter directed thrombolysis (pharmacologic or pharmacomechanical), surgical thrombectomy, endovascular stent placement, and rarely IVC filter placement. Evaluation for VTE risk factors with subsequent reduction of exposure to the risk factors is recommended.

The aim of this review is to discuss the presentation and management options of pediatric VTE with specific emphasis on the role of the interventional radiologist in management. An underlying aim will also be to highlight the importance of communication, collaboration, and multidisciplinary management between the various pediatric specialists (emergency medicine, diagnostic radiology, interventional radiology, hematology, intensive care, cardiology, etc) involved in the care of children affected by VTE.

## Preprocedural Evaluation and Management

Typically all patients present with pain or functional complaint in the body region associated with the thrombosis

*Abbreviations:* CBC, complete blood count; CDT, catheter directed thrombolysis; CNS, central nervous system; DVT, deep vein thrombosis; FFP, fresh frozen plasma; INR, international normalized ratio; IVC, inferior vena cava; PE, pulmonary embolus; PLT, platelet; PMT, pharmacomechanical thrombolysis; PT, prothrombin time; PTT, activated partial thromboplastin time; SVC, superior vena cava; ULN, upper limit of normal; VTE, venous thromboembolism

*Emory University School of Medicine, Department of Radiology and Imaging Sciences, Division of Interventional Radiology and Image-Guided Medicine, Atlanta, GA.

†Aflac Cancer and Blood Disorders Center of Children's Healthcare of Atlanta, Atlanta, GA.

‡Emory University School of Medicine, Department of Pediatrics, Atlanta, GA.

Conflict of Interest: No conflict of interest to disclose from either participating author. KNP: Independent Data Monitoring Committee member for Daiichi Sankyo.

Address reprint requests to Anne E. Gill, MD, Emory University School of Medicine, Department of Radiology and Imaging Sciences, Division of Interventional Radiology and Image-Guided Medicine, 1405 Clifton Rd NE, Atlanta, GA 30322. E-mail: anne.gill@emory.edu

 https://doi.org/10.1053/j.ro.2019.06.003
0037-198X/

**Table 1** Anticoagulants* and Thrombolytics That May Be Considered for Use in Pediatrics

| Anticoagulants and Thrombolytic Medications | Example of Specific Medications |
|---|---|
| Unfractionated heparin | |
| Low molecular weight heparin | Enoxaparin, dalteparin, fondaparinux |
| Warfarin | |
| Tissue plasminogen activator (TPA)† | |
| Direct thrombin inhibitors | Argatroban, Bivalirudin, Dabigatran |
| Direct oral anticoagulants (Factor Xa inhibitors)‡ | Apixaban, Edoxaban, Rivaroxaban |

*All anticoagulants in pediatrics are consider off label use.
†Systemic vs catheter directed (+/− mechanical thrombolysis).
‡Current ongoing clinical trials in pediatrics.

(ie, chest pain, shortness of breath, leg/arm pain, difficulty bearing weight on extremity, or swelling). If the chief complaint is a swollen and painful extremity, the first screening test is often a Doppler US of the affected limb. Ultrasound can provide the diagnosis quickly and can help determine the degree of occlusion (partial vs complete). If the entire course of the thrombus can be visualized with US and normal patent vein is visualized central and peripheral to the thrombus, there is usually no need to proceed with further imaging of the more central veins (ie, IVC or SVC). However, if clot burden extends into the more central veins of the body such as the subclavian, brachiocephalic, and SVC (or external iliac, common iliac, and IVC), a contrast-enhanced computed tomography (CT) or magnetic resonance imaging (MRI) is necessary to accurately define the extent of thrombus. A high quality MRI is typically preferred to decrease radiation to pediatric patients. If there is suggestion of extension of clot into the central chest or abdominopelvic veins, it is imperative to image these vessels prior to intervention.

Pulmonary embolic (PE) disease is best imaged with a CT angiogram of the chest; MRA of the chest is often too motion degraded to give reliable information regarding the clot burden in the pulmonary arteries. Particular care must be taken to verify the study is obtained during the optimal phase of contrast with complete opacification of the pulmonary arteries. The location of the PE(s) and the size of the PE will help determine whether thrombolysis is necessary.

Once the area of thrombus is accurately identified, the hematology team is contacted and reviews the patient's best anticoagulation options (Table 1). Additionally, the hematology team typically discusses the more complex cases with interventional radiology (IR) to reach a decision whether the patient is a candidate for thrombolysis and/or thrombectomy. The patient must be carefully evaluated to see whether they can safely receive tissue plasminogen activator (tPA) (Table 2). If the selection criteria for tPA administration are met, the patient is then scheduled for a thrombolysis/thrombectomy procedure in IR. Prior to initiation of any therapy, assessment of baseline labs such as CBC, PT, PTT, fibrinogen, d-dimer, Bun/Cr, and pregnancy test are recommended. The need for thrombophilia evaluation should be discussed with hematology as some labs can be affected by acute thrombosis and other factors postprocedure if transfusions occur.

**Table 2** Risk Factors for Pediatric VTE*

| Anatomic | Clinical | Genetic | Other |
|---|---|---|---|
| • May-Thurner syndrome | • Antiphospholipid antibody syndrome | • Antithrombin deficiency | • Elevated factor 8 |
| • Paget-Schroetter | • Cancer | • Dysfibrinogenemia | • Hyperhomocysteinemia |
| • Thoracic outlet syndrome | • Central lines | • Factor V Leiden | • Smoking |
| • Tumor compression | • Congenital heart disease | • JAK2 mutation | |
| | • Estrogen therapy | • Paroxysmal nocturnal hemoglobinuria | |
| | • Family history of thrombosis | • Protein C deficiency | |
| | • Immobility | • Protein S deficiency | |
| | • Infection | • Prothrombin gene mutation | |
| | • Lupus or other autoimmune disease (eg, inflammatory bowel disease) | | |
| | • Nephrotic syndrome | | |
| | • Obesity | | |
| | • Pregnancy | | |
| | • Severe dehydration | | |
| | • Surgery | | |
| | • Trauma | | |
| | • Travel | | |

*Other risk factors exist, listed are more frequently found or risk factors to not miss.

# Deep Venous Thrombosis of the Extremity

## Clinical Presentation

In children with DVT, the most common presenting symptoms of an acute (<2 weeks duration of symptoms) DVT include pain and swelling of the affected extremity. Decreased or inability to use the extremity secondary to pain is also commonly reported. In children with clot provoked and propagated along a central line, line dysfunction may be the presenting symptom. Though less frequently reported, the following symptoms in the correct clinical context (acute or chronic duration of symptoms) may also warrant evaluation for thrombosis: cramping/tingling, prominent varicosities, dilated superficial or collateral veins, or color changes of an isolated extremity. DVT may also be "asymptomatic" and found incidentally on imaging performed for other indications.

## Risk Factors

Identification of risk factors for DVT are crucial. Elimination or reduction of the ongoing risk factors may aid in decreasing clot propagation and recurrence. The most common risk factor for thrombosis in children is central lines. They have been reported to be present in up to 85% of children with DVT.[7] In Table 2, additional risks factors are listed. When possible, removal of a provoking risk factor should be attempted, for example cessation of estrogen therapy or smoking and treatment of underlying conditions such as lupus should ensue.

## Patient Selection for Thrombolysis

There are no randomized controlled trials in pediatrics with regards to catheter-directed thrombolysis (CDT) for DVT of the extremity. Guidelines using lower grade evidence and expert consensus guidelines exist from American College of Chest Physicians, American Society of Hematology, American Heart Association, and other groups.[3,7,8] Clinical situations in which CDT is generally agreed upon are the following scenarios: massive and submassive PE, bilateral renal vein thrombosis with renal impairment, life or limb threatening VTE, mobile right atrial thrombus >2cm, Kawasaki disease with giant aneurysms and acute coronary artery thrombosis, SVC syndrome, and shunt obstruction in children with congenital heart disease. Some groups also recommend consideration of thrombolysis in acute iliofemoral or IVC thrombosis and anatomic compression syndromes (May-Thurner and Paget-Schroetter/Thoracic Outlet Syndrome).[10-13]

The authors' general approach to evaluation for thrombolysis: Consider CDT in thrombosis that threatens life, limb and/or organs. Life threatening thrombosis includes massive/submassive PE, cardiac shunt thrombosis, and coronary artery thrombosis. Limb threatening venous thrombosis is defined as severe IVC/iliofemoral (suprainguinal) thrombosis. Severe IVC and iliofemoral thrombosis are defined as significant clot burden without improvement in symptoms on standard anticoagulation or those with Phlegmasia cerulea or alba dolens regardless of supra- or infrainguinal location of thrombosis.[14,15] Additional situations where CDT therapy is beneficial include extremity anatomic compression syndromes (May-Thurner syndrome, Venous Thoracic Outlet/Paget-Schroetter syndrome); while these entities are not necessarily limb threatening, the severe external compression of the vessel(s) limits the responsiveness to anticoagulation alone.[13] Of note patients with evidence of extremity compartment syndrome warrant urgent evaluation and may need urgent fasciotomies and other considerations that are beyond the scope of this review. Finally, organ threatening thrombosis is defined as bilateral renal vein thrombosis or SVC thrombosis. Discussion of bleeding risk and other morbidities is warranted as well prior to initiation of any anticoagulant or thrombolytic therapy not only with parents but among the medical providers involved in the patient's care. Table 3 lists our recommended exclusion criteria for thrombolysis.

**Table 3** Conditions in Which Thrombolysis Should Not Be Considered or Needs Further Discussion With Interventional Radiology

- Known tPA allergy.
- Any active bleeding.
- Major general surgery within 7-14 days (depends on type, consult IR to assess risk vs benefit).
- CNS ischemia/bleed/neurosurgical procedure within 10-14 days.
- Invasive procedure within 3 days.
- Seizures within 48 hours (discuss with IR to assess risk vs benefit).
- Recent, severe trauma.
- Inability to correct severe coagulopathy: PTT $>$ 2$\times$ ULN or INR $>$ 1.5, PLT $<$ 50, fibrinogen $<$ 100 mg/dL.
- Pregnancy.
- Careful consideration in premature infants, patients with hypertension, or other risk factors for bleeding.
- Children with superficial venous thrombosis.

## Procedural Technique for Extremity Venous Thrombolysis

Once the patient is deemed safe for thrombolysis/thrombectomy, the patient is brought to the IR suite and the procedure is done under general anesthesia. It is the authors' preference and current practice model that systemic anticoagulation is continued during the procedure. The site for venous access is chosen; the goal is to obtain access into a nonthrombosed vein that is peripheral to the site of thrombus. For example, if the DVT involves the left femoral, external iliac, and common iliac veins; the ideal location for endovascular access is the nonthrombosed, left popliteal vein. In the setting of venous thoracic outlet syndrome, access is typically obtained in the brachial or basilic vein. Once endovascular access is stabilized, a gentle venogram can be performed to identify the extent of the clot and any venous collaterals draining the extremity. Wire access is then achieved across the clot and pharmacomechanical thrombolysis (PMT) is initiated.

While systemic thrombolysis therapy can be beneficial, there are several studies promoting the efficacy and benefit of

CDT to decrease the systemic risks of nontarget bleeding and PTS within the affected extremity.[16-18] The combined ability to perform CDT with PMT is recognized as the standard for rapid clot lysis in the adult population, and its safety has been shown in adolescents.[9,12] Concomitant CDT and PMT may reduce overall dose of thrombolytic agents as well as potentially decrease bleeding risk; thus, making it an attractive treatment despite limited data.[19] There are several available devices which are used for PMT, although all of the devices are considered off-label use in the pediatric population. The size of the device and technical expertise limit the use of PMT in neonates and small children.[19] Some of the most commonly used devices include AngioJet Rheolytic Thrombectomy System (Boston Scientific, Marlborough, MA), Trellis (Bacchus Vascular, Santa Clara, CA), CLEANER rotational thrombectomy device (Argon Medical Devices, Frisco, TX), and EkoSonic Endovascular System (EKOS, Bothell, WA). In the author's practice, AngioJet is the device most often used due to its small caliber, decreased risk of damage to the native venous valves, and overall familiarity with the product in our hospital system.

A weight-based bolus dose (0.1-0.3 mg/kg, maximum dose of 10 mg) of tPA is evenly dispersed throughout the clot burden using the Angiojet catheter "PowerPulse" mode. The tPA is allowed dwell within the thrombosed system (15-30 minutes) and then the device is switched to thrombectomy mode. During thrombectomy mode, the catheter is moved in an antegrade and retrograde fashion while the catheter is rotated through the clot. The rotation is thought to help the catheter "windows" remove as much clot from the entire lumen of the vessel. Mechanical disruption with angioplasty balloons is then performed in an effort to disrupt residual clot burden along the periphery of the vessel not previously aspirated by the Angiojet device. Angioplasty balloons are always sized to the vessel based on the preprocedure measurements (from MRI or CT) or periprocedure venograms.

Intravascular ultrasound (IVUS) is a very useful device to assess residual clot burden after PMT, particularly when the patient demonstrates an anatomical compression syndrome such as May-Thurner syndrome or Venous Thoracic Outlet syndrome. IVUS gives a 360° view of the vein and any residual thrombus is noted as echogenic material within the lumen (Fig. 1A) and if the vein is completely patent following the thrombolysis the vessel appears anechoic (Fig. 1B). In anatomic compression syndromes, IVUS can confirm the diagnosis in real-time: the point of maximal compression can be precisely located and the vessel diameter accurately measured.[17,20] If there is severe external compression of the left common iliac vein, an endovascular stent may be indicated in adolescent patients who have reached skeletal maturity. If the area of external compression is not relieved, the patient is at risk of rethrombosis of the vessel despite adequate anticoagulation during the initial procedure/hospitalization. Additionally, relieving the outflow obstruction by stent placement in the common iliac vessel allows for improved venous outflow from the thrombosed extremity, eliminates the future complications from residual hyaline scar material within the vein lumen from chronic microtrauma, may shorten the duration of further CDT, and

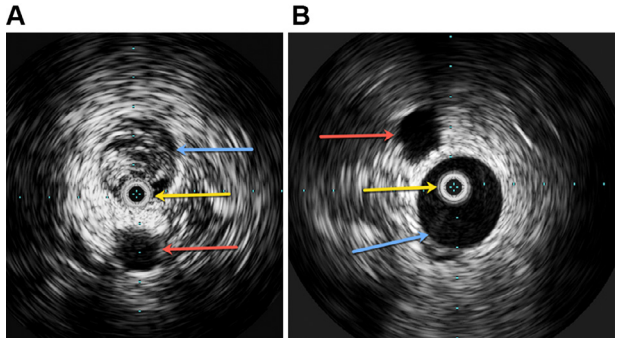


**Figure 1** A 16-year-old female presented with thrombosed right lower extremity deep venous system extending from popliteal vein to the right common iliac vein. (A) Intravascular ultrasound (IVUS) of the right common iliac vein shows the vessel lumen filled with echogenic material representing occlusive clot (blue, solid arrow), the IVUS transducer within the lumen of the vessel (yellow, solid arrow), and the right iliac artery (red, solid arrow). (B) After 24 hours of catheter directed thrombolysis (CDT), IVUS demonstrates patency in the right common iliac vein (blue, solid arrow), IVUS transducer (yellow, solid arrow), and the right iliac artery (red, solid arrow). (Color version of figure is available online.)

decreases risk of rethrombosis.[21] Therefore, it the author's opinion that endovascular stent placement during the first thrombolysis procedure decreases the duration of CDT infusion time as well as risk for recurrent clot formation. Finally, in the setting of venous thoracic outlet syndrome, there is virtually never an indication for endovascular stent placement, and all patients should be followed by/referred to a vascular or general surgeon for first rib resection or other surgical correction after successful thrombolysis.

The ideal endovascular stent for external compression of the iliac veins is a one with a low profile, precise deployment, and strong radial force. Stent choices typically include nitinol stents such as, Wallstent (Boston Scientific, Marlborough, MA), Protégé (Medtronic, Minneapolis, MN), SMART (Cordis Corporation, Bridgewater, NJ), and Zilver (Cook Medical, Bloomington, IN). While the Wallstent has the strongest radial force, it can foreshorten during deployment and balloon dilation. In less experienced operators, the stent foreshortening may leave a portion of the vein still affected by the right common iliac artery, leaving the patient at risk for recurrent symptoms. However, if the operator can accurately account the foreshortening, the Wallstent seems to be strongest and the most flexible for the curves within the deep pelvis. Otherwise, the Protégé or Zilver stents are easier to precisely deploy across the area of compression but have less radial force than the Wallstent. The position of the stent, stent apposition to the vein wall, and patency are re-evaluated with IVUS (Fig. 2). For operators that are not as comfortable using IVUS, a repeat venogram is performed.

After PMT and angioplasty are performed, regardless of whether an endovascular stent is placed, the infusion catheter is carefully positioned with fluoroscopic guidance for CDT. The infusion catheter is placed over the wire across the entire burden of clot. The working wire is removed and, depending on the type of infusion catheter placed, the occlusion wire is

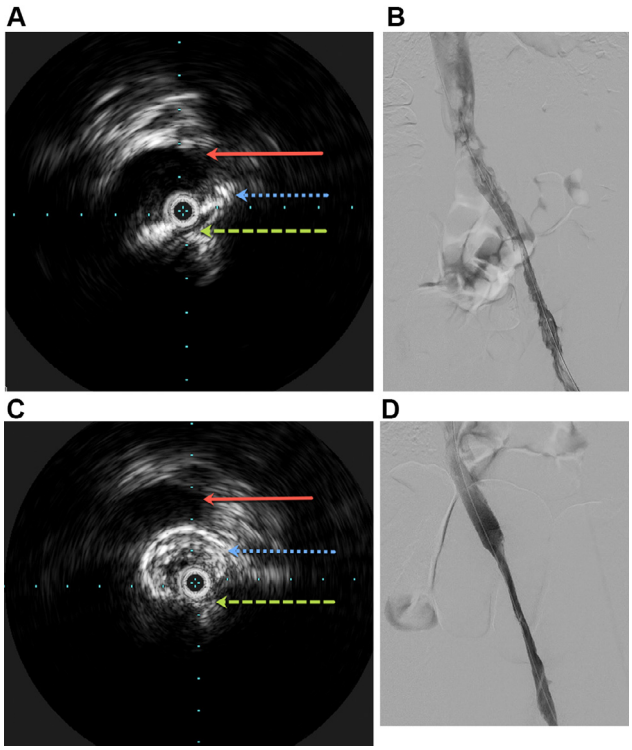


**Figure 2** A 16-year-old male presented with thrombosed left lower extremity deep venous system extending from the popliteal vein to the left common iliac vein (LCIV) and MRV of the pelvis demonstrated severe external compression of the LCIV by the overriding right iliac artery. (A) IVUS of the left common iliac vein demonstrates the severe compression of the LCIV (right iliac artery with red, solid arrow; LCIV compression with blue, dotted arrow; anterior cortex of the vertebral body with green, dashed arrow). (B) Corresponding venogram through the LCIV with residual intraluminal clot after pharmacomechanical thrombolysis and balloon angioplasty. (C) IVUS of the LCIV after stent deployment shows persistent thrombus but resolved external compression of the LCIV (right iliac artery with red, solid arrow; stented LCIV with blue, dotted arrow; anterior cortex of the vertebral body with green, dashed arrow). (D) Follow-up venogram after 24 hours of CDT shows improved caliber of iliac vessels, patency of the LCIV and stent, with excellent flow through the vessels. (Color version of figure is available online.)

placed through the catheter allowing the medication to seep through the infusion pores rather than through the catheter end hole. The ideal goal for the infusion catheter positioning is to have the tip in a patent, central vein (usually either the IVC or SVC) and the distal portion in the patent, peripheral vein (usually the distal femoral or brachial veins). The dose for tPA is calculated and the medication is delivered via an IV infusion pump at the determined rate. At our institution, tPA is infused at a rate of 0.03-0.06 mg/kg/h with a maximum of 1 mg/h. If 2 infusion catheters are placed, the dose is split between both catheters.

The infusion catheter is safely secured to the skin and lines are clearly labeled. The low dose heparin infusion is initiated through the vascular sheath at the venous access site. The low-dose heparin (2 units/mL usually running at 50 units/h in most adolescent patients) is to keep the potential space between the vascular sheath and the infusion catheter free of clot. It is imperative that the primary team understand this heparin is not systemic anticoagulation for the patient. Additionally, in smaller, younger patients the dose of heparin in the vascular sheath must be carefully calculated so as not to cause volume overload nor heparin overdose (exceed the systemic anticoagulation or prophylaxis goals). The patient is transferred from the IR suite to the intensive care unit for overnight CDT and postprocedure management and care.

## Immediate Postprocedural Patient Management

After initiation of thrombolytic therapy, the patient should remain on low dose heparin to prevent clot recurrence or propagation. We recommend unfractionated heparin drip at 10 units/kg/h. We do not routinely monitor PTT or heparin Anti-Xa activity at this low dose but this decision to monitor for heparin activity should be made by the hematologist. We recommend that a patient undergoing thrombolysis be monitored closely for thrombolysis efficacy as well as for potential side effects, in particular bleeding. tPA causes fibrinolysis, fibrinogenolysis and postmechanical thrombectomy hemolysis, and hemoglobinuria (with possible increase in creatinine/acute kidney injury). As a result of these expected findings, monitoring hemoglobin, hematocrit, fibrinogen activity, BUN, creatinine, and platelets is recommended. Additionally, frequent monitoring of d-dimer and fibrinogen can provide evidence of efficacy of thrombolysis. At our institution, these labs are monitored Q6-8 hours, adjusting as needed based on lab results. Postinitiation of thrombolysis, the d-dimer should increase and fibrinogen will decrease. The authors' aim is to keep fibrinogen activity >100 mg/dL and platelets >100 ($\times 10^9$/L) for adequate hemostasis (based on pediatric thrombolysis literature and expert consensus); if fibrinogen levels are below the goal, and hemoglobin is maintained, repletion with cryoprecipitate is recommended.[22,23] Additionally, if d-dimer is not increasing on post-thrombolysis monitoring, thrombolysis may be ineffective or suboptimal and increasing the tPA dose or repletion of plasminogen (via transfusion of FFP) should be considered. Monitoring of plasminogen activity is not routinely done in most institutions as it is not an available test, however, in institutions with the capability to monitor real time plasminogen activity it may be beneficial to monitor particularly if other indicators of thrombolysis efficacy are not seen and in prolonged (>24 hours) thrombolysis. Throughout the thrombolytic infusion, the patient should have frequent assessments of the affected extremity for vascular changes and ensure adequate perfusion. Additional supportive care that we often consider include preprocedure placement of Foley catheter, adequate hydration pre-, during-, and postprocedure, bed rest during tPA infusion, no arterial sticks nor intramuscular injections, pain control as needed, avoidance of NSAIDs or other antiplatelet medications (which may increase the bleeding risk), and avoidance of any procedure that can increase risk of bleeding. Compression stockings can be considered as well.

### Procedural Course for Extremity Lysis Check and Post-thrombolysis Patient Management

After 12-24 hours of the low-dose tPA infusion, the patient is returned to IR for post-CDT venography to assess progress and determine whether CDT should be continued or terminated. The infusion catheter and occlusion wire are carefully removed from the patient and venograms performed through the vascular sheath. If there is poor opacification of the central veins, a diagnostic angiography catheter may be necessary to clarify the presence or absence of clot centrally (in the IVC or SVC). Finally, IVUS may be used to confirm resolution of clot burden and confirm patency. Once the majority of clot burden has cleared and the flow through the deep venous system is no longer compromised, CDT can be terminated. Clinically, once adequate clot resolution has been achieved, the patient's extremity appears less swollen, demonstrates improved capillary refill times, and there is less pain. If these parameters are not met, the infusion of low-dose tPA should be continued for another 12-24 hours. It is unusual for low-dose tPA therapy to be necessary or beneficial after infusion for longer than 48-72 hours; at that point, in the author's opinion, the risk to the patient for spontaneous bleeding or other complications outweighs the benefit of continuing thrombolysis. Surgery is rarely the first intervention for acute iliocaval (or cavoatrial) DVT.[24] However, if the clot burden does not improve with CDT, vascular surgery should be consulted as surgical thrombectomy may be warranted/necessary.

Once the infusion catheter is removed, the patient is transferred back to the intensive care unit. Over the next 24-48 hours the patient's systemic anticoagulation will be transitioned from heparin drip to an outpatient regimen (typically enoxaparin). Once stable, the patient is transferred from the intensive care unit to the hematology unit and any additional labs or teaching can occur. The patient is then scheduled for follow-up clinic appointments with the thrombosis and IR clinics. In pediatric patients with venous thoracic outlet syndrome, the vascular surgery team should be consulted while patient is in the hospital and follow-up appointment scheduled. Follow-up imaging should also be considered at the time of discharge. Usually extremity Doppler ultrasound is scheduled for 1 month and 3 months after thrombolysis/stenting. If there is concern for stent or vessel patency on the ultrasound exam, a follow-up MRI or diagnostic venogram can be considered.

## Pulmonary Embolism

### Clinical Presentation

In children with PE, the common presenting symptoms include chest pain, cough, tachypnea, and dyspnea.[17] Back pain, fatigue, hemoptysis, tachycardia, dyspnea on exertion, and presyncope or syncope may also be reported in children with PE. PE can present with cardiovascular compromise ranging from mild heart strain to cardiovascular collapse and/or death. While death and cardiovascular collapse are not common, it is not uncommon for a PE to be clinically "silent" (ie, lack of classic symptoms) or to be found in context of other pathologic processes (such as, pneumonia, ARDS, acute chest, and others) which may decrease initial index of suspicion for PE diagnosis.[25,26] PE may occur in isolation but is often secondary to embolism from an extremity and as such special attention for evaluation for signs and symptoms of extremity DVT are also recommended.

### Risk Factors

Identification of risk factors for PE are important to prevent clot propagation and recurrence. The risk factors for PE are similar to DVT (Table 2). Additionally, there is data to suggest that black children may have higher odds of developing PE.[5]

### Patient Selection for Pulmonary Artery Thrombolysis

After a diagnosis of PE is confirmed, evaluation of the 4 extremities should be undertaken even if no signs or symptoms of DVT are present as this may alter decision-making for therapeutic strategies. Risk assessment for bleeding should be done prior to initiation of therapy. In adult patients with PE, there is data to suggest risk categories, based on degree/location of obstruction and cardiovascular compromise, determine which therapeutic strategies are utilized.[27,28] Data for this approach is lacking in children with PE though pediatric hematologists, pediatric interventional radiologists, and others pediatric specialists, in their expert opinion, may follow a similar risk based strategy for intervention. Some pediatric institutions have developed PE response teams to facilitate/optimize management of the children with PE.[25] Anticoagulation alone or CDT and systemic anticoagulation may be considered in the management of children with PE.

With regards to the selection of children with PE who may qualify for thrombolysis, guidelines using lower grade evidence and expert consensus exist from American College of Chest Physicians, American Society of Hematology, American Heart Association, and other groups.[3,7,8] Generally agreed upon metrics to suggest CDT include massive and submassive PE or PE causing cardiovascular compromise (tachycardia, hypotension, right heart strain as evidenced by dilated right ventricle (RV) and/or tricuspid regurgitation). Discussion of risk of bleeding and other morbidities amongst specialists involved in the management of the child with PE is warranted prior to initiation of any anticoagulant or thrombolytic therapy. Table 3 lists suggested exclusion criteria for thrombolysis.

### Procedural Course for Pulmonary Artery Thrombolysis

Once the PE has been characterized, the metrics for thrombolysis have been verified, and the patient is deemed safe for

thrombolysis/thrombectomy; the patient is brought to the IR suite for induction of general anesthesia. It is the author's preference and current practice that systemic anticoagulation is continued during the procedure. There are 2 possible sites for peripheral venous access: right internal jugular vein vs right femoral vein and either site can provide adequate access into the pulmonary arteries via the right heart. It is the authors' preference to use the right femoral access as it is usually more comfortable for the patient (no catheters are coursing through the neck). However, anatomical considerations must be taken into account including patency of the vessel chosen (no femoral DVT present), history of congenital heart disease with atypical connection of the SVC to the right atrium, history of discontinuation of the IVC from IVC agenesis vs azygous continuation, or surgical reconstruction of the IVC during a liver transplant.

Once the access is obtained, an angled or shepherd's hook shape catheter is used to cross from the right heart into the main pulmonary artery. The authors' catheter and wire combination preference for crossing the right heart into the pulmonary artery is a 5F Contraflush catheter (Boston Scientific, Marlborough, MA) and a stiff, hydrophilic wire (Glidewire). With the hydrophilic wire in the main pulmonary artery, the catheter is advanced to obtain more stable access into the more distal pulmonary artery.

The catheter is positioned within either the right or left pulmonary artery and pressure measurements are obtained. The pulmonary artery system freely communicates between the right and left side; if there are significantly elevated pressures on the right side, due to occlusive thrombus, the left pulmonary artery pressures may also be elevated despite the presence or absence of thrombus burden (Fig. 3). Normal, mean pulmonary artery pressures in children range from (15-24 mmHg); therefore, anything above 25 mmHg is considered elevated. Usually, the degree of clot burden directly correlates with the degree of pulmonary artery pressure elevation.

Pulmonary artery angiograms are then obtained with the multiside hole flush catheter positioned in the right or left main pulmonary artery and then the catheter is positioned in the vessel not previously imaged. All pulmonary artery angiograms are performed with breath-holds by the anesthesia staff. If the child is less than 20 kg, a hand injection angiogram will suffice; however, if the child is greater than 20 kg, a power injector is connected to the catheter and an injector is used to deliver contrast in a continuous supply for the angiogram. It is imperative that the correct parameters are chosen in children for the power injection and typically range from 6-10 mL per second for 10-20 total mLs (smaller volumes and shorter injection times are used for smaller patients and vice versa). Finally, in order to best visualize the pulmonary artery anatomy, it is recommended the angiograms are obtained in LAO and RAO oblique. When reviewing the pulmonary artery angiograms, it is important to visualize and document the anatomic location of the clot burden as well as the severity of compromised lung perfusion (Fig. 3).

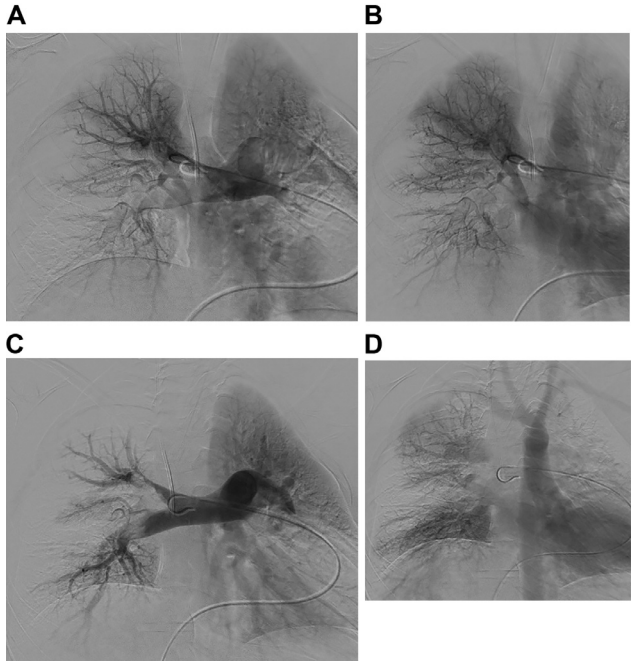


**Figure 3** An 18-year-old female presented after a syncopal event to the children's hospital and was found to have a massive PE in the right main pulmonary artery. Early (A) pulmonary artery angiogram demonstrating the profound clot burden in the right main pulmonary artery extending into the interlobar artery and distal branches. Contrast refluxes into the left main pulmonary artery. On the late angiogram (B), there is adequate perfusion of only the upper lung zone with significantly decreased perfusion of the middle and lower lung zones (pulmonary artery mean pressure measurement 30 mmHg). CDT was initiated and monitored for 18 hours and then she was brought back for the lysis check. Early (C) and late (D) pulmonary artery angiograms show dramatic improvement in the degree of clot burden in the right pulmonary artery system as well as the perfusion of the lung (pulmonary artery mean pressure measurement 27 mmHg). Despite the small residual clot, the patient was very much improved (no longer requiring pressors, ventilator settings decreased) that the decision was made to terminate CDT.

Once the clot burden is defined, a hydrophilic wire is advanced past the clot burden into a distal branch of the pulmonary artery. If the position of the wire can be maintained, without losing the access across the clot burden, the catheter can be exchanged for the infusion catheter at this point. However, if the operator fears the access might be lost with the stiff hydrophilic wire, it is best to exchange for a more stable, less slippery wire such as a Rosen wire which will not cause damage to the adjacent pulmonary vasculature (gentle, curved tip) and will not lose access (short floppy end with remainder of wire that is stiff). The infusion catheter is then carefully advanced over the wire and positioned so the infusion holes span across the clot from the patent, distal pulmonary artery branch to the patent main pulmonary artery. Careful consideration must be paid when choosing the infusion length of the catheter. Usually children will require a 10 cm infusion length in the pulmonary arteries, but adolescents and larger clot burdens may require longer lengths. The working wire is removed and replaced with the

occlusion wire. The dose for tPA is calculated and the medication is delivered via an IV infusion pump at the determined rate (see institutional dose limits above).

If the pulmonary artery thrombus is bilateral, the total dose of tPA must be split between 2 infusion catheters (typically 0.5mg/h/catheter unless a smaller dose is warranted by the patient's weight). Additionally, if the clot burden is most severely affecting 1 side than another, the first infusion may be to address the more severely affected side with the plan to address the less severely affected side at the follow-up lysis check. Mechanical thrombectomy is not thought to add any additional benefit in children or adolescents due to the risk of showering the more distal pulmonary artery branches with thrombus and limiting the chances the clot will clear with flow mediated thrombolysis.

In selected instances such as contraindication to tPA, suction thrombectomy can be beneficial either as a concomitant treatment with or following tPA thrombolysis or suction thrombectomy alone. A critical consideration in deciding to use suction thrombectomy is the size of the catheter necessary to remove clot. In the authors' institution, the Indigo system (Penumbra, Alameda, CA) is used and in order to adequately engage clot burden in the pulmonary arteries either a 5F or 8F system is necessary. Similarly, the expected volume of blood loss from suction thrombectomy must be estimated and deemed acceptable for the size of the patient. In these instances, blood transfusion during the procedure may be needed. If appropriate, suction thrombectomy can be used as an initial treatment prior to thrombolysis or following tPA bolus infusion once the clot has softened. The staged thrombolysis or thrombectomy plan should be discussed between IR, hematologists, anesthesiologists, and intensivists to ensure a clear plan is created for the critically ill patient.

The same process for securing the thrombolysis infusion catheter(s) to the skin, labeling of lines, and infusing low dose heparin through the vascular sheath is undertaken (please see procedural course for extremity DVT thrombolysis for more detail). The patient is transferred from the IR suite to the intensive care unit for postprocedure management and care.

### Immediate Postprocedural Patient Management

The post-thrombolysis procedural management follows the same course as for postprocedural DVT thrombolysis management (see above).

### Procedural Course for Pulmonary Artery Lysis Check and Post-thrombolysis Patient Management

After 12-24 hours of the low-dose tPA infusion, the patient is returned to IR for the lysis check to determine whether the infusion should be continued or terminated. The occlusion wire(s) is carefully removed from the patient, replaced by a stiff guidewire, and the infusion catheter is exchanged for a multisidehole catheter. Pulmonary artery pressures are measured and compared to the prethrombolysis pressures. Pulmonary artery angiograms are repeated with breath holds and typically using the power injector. Angiograms are compared to the prethrombolysis angiograms. If clot burden has significantly decreased, lung perfusion is improved, and pulmonary artery pressures are improved; CDT can be discontinued (Fig. 3). However, if 1 of the above parameters (clot burden, lung perfusion, or pulmonary artery pressures) remain significantly compromised; it is in the best interest of the patient to continue thrombolysis for another 12-24 hours if there are no markers of deleterious side effects from the tPA administration. Low-dose tPA infusions are typically continued for no longer than 48-72 hours. If the clot burden does not improve with CDT and/or suction thrombectomy, vascular surgery should be consulted as surgical thrombectomy is often warranted/necessary in order for short-term clinical improvement and decrease the long-term risk of pulmonary artery hypertension. Very few centers provide pediatric pulmonary artery thrombectomy; however, they should be pre-emptively contacted with prospective patients once it becomes clear that patients are not responding as hoped to the minimally invasive procedure(s) (Fig. 4).

Once the infusion catheter is removed and a sterile dressing placed at the venous access site, the patient is transferred back to the intensive care unit. Over the next 24-48 hours, the patient's systemic anticoagulation will be transitioned from heparin drip to outpatient regimen (typically enoxaparin). Once stable, the patient is transferred from the intensive care unit to the hematology unit and any additional labs or teaching can occur. The patient will need follow-up clinic appointments with the thrombosis, pulmonary hypertension, and IR clinics. Follow-up imaging should also be considered at the time of discharge. Typically, chest CT pulmonary angiogram is done at 6 months after the procedure.

## IVC Thrombosis

### Clinical Presentation

In children with IVC thrombosis, the thrombus may be isolated or contiguous with thrombi in distal veins. In registry data, thrombosis of the IVC was seen in 10% of children.[29] The common presenting symptoms include extreme, severe symptoms of DVT when IVC and veins peripheral to IVC are concomitantly thrombosed. It is not uncommon for the extremity to appear much more compromised (profound duskiness, pain, swelling, and delayed capillary refill) when there is associated IVC thrombosis as compared to an extremity with DVT that does not extend to the IVC.

IVC thrombosis at the level of the renal veins may present with renal insufficiency or hematuria if clot extends into the renal veins. In isolated IVC thrombosis which are most often due to central line placement, line dysfunction may be present as well as swelling of 1 or both extremities. Another presentation of IVC thrombosis in children that have congenital IVC agenesis or atresia, which may or may not present in

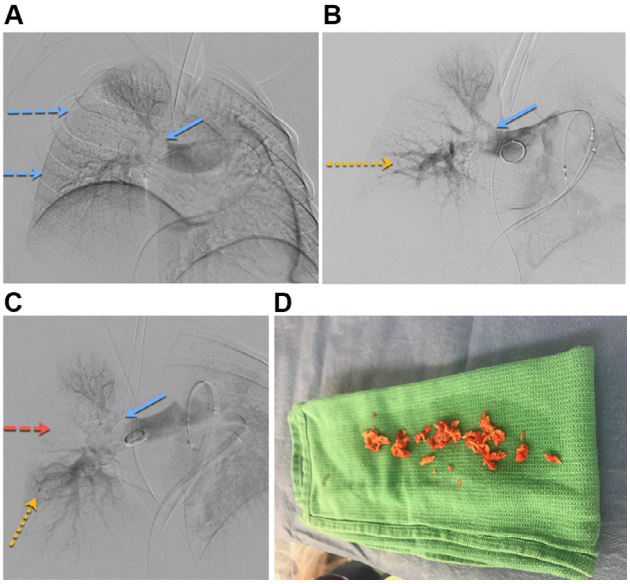


**Figure 4** A 19-year-old female presents with left lower extremity DVT and bilateral pulmonary emboli. Day one (A) pulmonary artery angiogram demonstrating large clot burden in the right main pulmonary artery (solid blue arrow) with poor perfusion of the middle and lower lung zones (dashed arrows). Small right pleural effusion. Right pulmonary artery angiogram after 18 hours of CDT (B) with persistent large clot burden in the main right PA (solid arrow) but improved perfusion at the right lung base (dashed arrow); decision was made to continue CDT. Repeat right pulmonary artery angiogram after 36 hours of CDT (C) shows relatively unchanged clot burden in the right main PA (solid arrow), improved perfusion of the right lung base (short dash arrow) but no improvement in the right middle lung zone (long dash arrow); decision made to terminate CDT. Patient was referred to vascular surgery for endarterectomy which required patient to be transferred to the adult hospital. (D) Chronic clot retrieved from the right main PA after pulmonary artery endarterectomy, which explains why the patient did not respond well to the CDT treatment. (Color version of figure is available online.)

infancy, is thrombosis which is often chronic and calcified or in adolescence with an unprovoked DVT of the lower extremity or PTS.[30-33] Signs and symptoms of PTS include chronic or intermittent pain, exercise induced pain, neuropathy, varicose veins, venous collaterals, leg swelling/edema, color changes of the leg, or venous stasis ulcers.[12,33] In the authors' experience in adolescents with agenesis of the IVC with chronic thrombosis, atrophy of proximal lower extremity muscle groups has been seen as well.

## Risk Factors

Identification of risk factors for thrombosis are important to prevent clot propagation and recurrence as well as to guide treatment options. The risk factors for IVC thrombosis are similar to PE and DVT (Table 2). IVC thrombosis may be associated with patients who have inherited thrombophilia(s) and/or may have been experiencing symptoms of DVT for more than 2-3 weeks. Additionally, these children may also have congenital venous anomalies like IVC atresia or agenesis, history of abdominal/vascular trauma or abdominal surgery.[30]

## Patient Selection for Thrombolysis

After a diagnosis of IVC thrombosis is confirmed, radiographic evaluation of the lower extremities and pulmonary arteries should be undertaken even if no signs or symptoms of DVT or PE are present; the findings may alter decision-making for therapeutic strategies. Risk assessment for bleeding should be done prior to initiation of therapy. As with DVT and PE, there are no randomized clinical trial data in children to suggest 1 treatment strategy (systemic anticoagulation alone or CDT with systemic anticoagulation) over the other; however, there are some studies with long-term follow-up to suggest that unresolved long standing IVC thrombosis has increased risk of developing PTS than those with IVC thrombosis resolution.[33] Additionally, thrombosis in the IVC at the level of the renal veins may increase risk of renal vein thrombosis which may lead to hematuria and renal dysfunction. Given these potential adverse effects/outcomes, there is expert opinion to suggest the use of thrombolysis is indicated in these situations.[8,30] Discussion of risk of bleeding and other morbidities amongst specialists involved in the management of the child with IVC thrombosis is warranted prior to initiation of any anticoagulant or thrombolytic therapy. Table 3 lists suggested exclusion criteria for thrombolysis.

Finally, the possibility of embolization of IVC clot to the pulmonary arteries or heart must be addressed. It is the authors' opinion while there are no clinical data to support the placement of IVC filters in pediatrics, IVC filters can provide a significant prophylactic benefit to decrease risk of thrombus embolization in the setting of IVC thrombus if the child/adolescent is deemed safe for placement or if there is contraindications to anticoagulation or thrombolysis. Of note, no reliable guidelines exist for placement of prophylactic filters in patients <18 years old.[34] Additionally, there is no data supporting placement of filters in patients less than 10 kg.[35] Only removable filters should be considered in pediatric patients with VTE and the filter removal should be scheduled at the time of placement. IVC filters may be placed for a few days (Raffini et al report some prophylactic filter placements for as little time as 21 days[34]) or up to 3-6 months post-thrombolysis depending on the patient's clinical course and the risk factors for residual or recurrent thrombus.[36]

## Procedural Course for IVC Thrombolysis

The decision algorithm to pursue IVC thrombolysis is essentially the same as for extremity DVT thrombolysis (please reference the DVT section above). The procedure is done under general anesthesia. Typically, an IVC filter is placed if the patient is >10 kg and the diameter of the IVC can accommodate such a device. A removable, nonpermanent IVC filter offer short-term prophylaxis against life threatening PE and minimize the long-term effects seen with permanent filters (increased risk of thrombosis in pelvic veins).[37] Either internal jugular or femoral/popliteal access is preferred for delivery of the IVC filter. The filter

must be placed central to the thrombosed IVC. Once the filter is in place, the thrombolysis procedure may begin. A separate access site may be required for the thrombolysis procedure. Wire access is then achieved across the clot; and if appropriate, PMT is initiated. There are very few studies demonstrating the efficacy and/or safety of using PMT for IVC thrombosis in pediatric patients with only a handful of cases using PMT in the IVC.[18,38] Considerations of patient total blood volume, diameter of IVC, and potential damage to the vessel sustained during PMT should be taken into consideration before deciding to proceed with PMT. If the patient is a neonate, infant, or small child, an alternative approach to PMT can be considered by administering a weight-based, bolus dose of tPA (1 mg/kg) hand injected through a multi-sidehole infusion catheter and then allowed to dwell for 12-15 minutes (Fig. 5). Clot maceration with angioplasty balloons is then performed in an effort to mechanically disrupt any residual clot burden along the periphery of the vessel. If a filter is in place, careful attention must be paid to manipulating the balloon with respect to the filter's tines.

Venograms (and IVUS, when appropriate) evaluation are performed throughout the thrombolysis process to verify the effect on the clot burden. Following PMT and/or clot maceration, the infusion catheter is positioned with the infusion holes crossing the clot to initiate CDT. The dose for tPA is calculated, and the medication is delivered via an IV infusion pump at the determined rate. All lines and sheaths are sutured to the skin and appropriately labeled. The patient is transferred to the intensive care unit for post-procedure management and care.

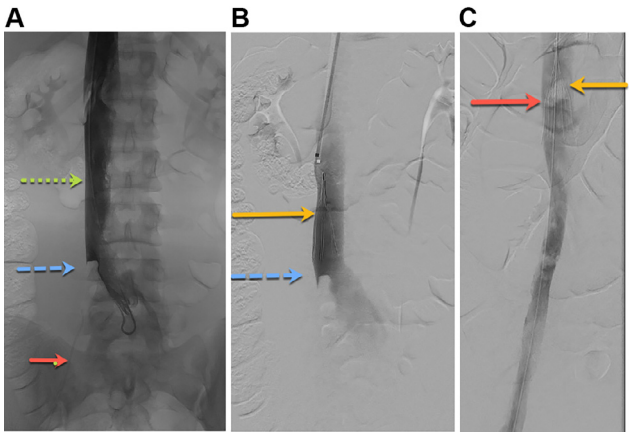


**Figure 5** A 17-year-old female presents with severe right lower extremity pain, swelling, and cyanosis with PE in the right interlobar pulmonary artery. (A) Venacavogram shows clot extending from right common iliac vein (RCIV) into the IVC (occluded RCIV red, solid arrow; IVC clot blue, dashed arrow; patent IVC green, dotted green arrow). (B) Filter deployed in the patent, infrarenal IVC (yellow, solid arrow) with clot in the RCIV. (C) Venacavogram after 24 hours of CDT and filter present shows improved patency of the RCIV and peripheral IVC with captured clot in the IVC filter (filter yellow, solid arrow; clot red, solid arrow). (Color version of figure is available online.)

### Immediate Postprocedural Patient Management

The post-thrombolysis procedural management follows the same course as for postprocedural DVT and PE thrombolysis management. Any changes in the patient's respiratory function, chest comfort, or neurologic status must be carefully heeded and imaging obtained to rule out pulmonary emboli.

### Procedural Course for IVC Lysis Check and Post-thrombolysis Patient Management

The patient is brought back to IR for the lysis check usually after 24 hours of thrombolytic infusion. Repeat venograms and IVUS can be performed to verify resolution of the thrombus. Further balloon angioplasty may be required to assist with clot maceration. If an IVC filter is present, the risk of embolization of clinically significant macerated clot is substantially reduced; however, there may be tiny fragments that can dislodge and travel to the pulmonary arteries but the impact of such small (subsegmental) clot is typically minimal and likely resolves with the systemic anticoagulation.

A particular challenge in IVC thrombolysis with an IVC filter is the restricted flow through the device which can delay clot clearance. Longer thrombolysis infusion times may be necessary and endovascular stenting may be necessary to retain normal lumen diameter, provide adequate flow, and achieve complete clot resolution. Suction thrombectomy is an alternative method for clearing IVC thrombus after it has softened from the tPA infusion (please refer back to DVT section for specifics regarding patient selection and considerations for this therapy).

Once the clot burden has resolved and CDT is terminated, the patient is transitioned from heparin infusion to an anticoagulation medication which can be administered in the outpatient setting. The patient will need follow-up clinic appointments with the thrombosis and IR clinics. The discharge plan for the patient must include the plan for filter removal. At the authors' institution, the patient is scheduled for bilateral lower extremity doppler ultrasound at 3 months after filter placement. Once the BLE and IVC are confirmed to be clot free, the filter is removed in IR.

## Superior Vena Cava Thrombosis

### Clinical Presentation

In children with thrombosis of the SVC, the thrombosis may be isolated or contiguous with thrombi in chest or upper extremity veins. In registry data of central venous catheter related thrombosis, thrombosis of the SVC was seen in 18.7% of children with VTE.[29] The common presenting symptoms of acute SVC thrombosis include: swelling of head or neck, swelling of upper extremity or chest, dyspnea, headache, and plethora.[39] Pulmonary emboli can easily occur as the result of SVC thrombi. SVC thrombi can also be initially asymptomatic and become chronic. Chronic SVC thrombosis can present with chronic head swelling,

intermittent pain or exercise induced pain in the upper extremity, neuropathy, varicose veins, venous collaterals, chronic or intermittent arm swelling/edema, and plethora.

It is important to differentiate SVC thrombosis and SVC syndrome. SVC thrombosis can cause SVC syndrome but not all cases of SVC syndrome are due to SVC thrombosis. SVC thrombosis may be nonocclusive and continue to allow the drainage of the distal veins, but when there is critical narrowing from stenosis, occlusive thrombosis, or external compression from tumors or other causes, the child can develop potentially life-threatening SVC syndrome.

## Risk Factors

Identification of risk factors for SVC thrombosis are important to prevent clot propagation and recurrence as well as to guide treatment options. The risk factors for SVC thrombosis are similar to DVT, PE, and IVC thrombosis (Table 2). Children with central venous catheters (either small bore PICC lines or hemodialysis catheters) or shunts (eg, ventriculoatrial) in the upper venous system are at highest risk of developing SVC syndrome. The long-term, central venous catheter usually leads to SVC stenosis which then compromises flow and eventually leads to occlusive clot formation. Similarly, patients with congenital heart disease who have undergone surgical interventions that manipulate the upper body venous system are also at high risk of developing SVC syndrome.[40]

## Patient Selection for Thrombolysis

After a diagnosis of SVC thrombosis is confirmed, determination of acuity of symptoms is paramount as this will guide the urgency and type of intervention. In the acute setting of SVC syndrome, urgent treatment is warranted. Appropriate imaging of the SVC and visualization of the upper extremity venous system as a whole is recommended to not only guide endovascular therapy but also to determine if there is an underlying etiology.

Risk assessment for bleeding should be done prior to initiation of therapy. As with all of the prior thrombosis subtypes discussed, there is no randomized clinical trial data to suggest 1 optimal treatment strategy (systemic anticoagulation alone, CDT and systemic anticoagulation, or endovascular stenting). However, there is data showing efficacy (maintained vascular patency) in patients who underwent stenting of the SVC at the time of SVC syndrome presentation.[41] Discussion of risk of bleeding and other morbidities amongst specialists involved in the management of the child with SVC thrombosis is warranted prior to initiation of any anticoagulant or thrombolytic therapy. Table 3 lists suggested exclusion criteria for thrombolysis.

## Procedural Course for SVC Thrombolysis

Once the extent of thrombus is determined from the CT or MRI, the plan for access site and patient positioning can be determined. All prior considerations discussed for DVT and IVC thrombolysis are taken into account, and the procedure is performed under general anesthesia. Typically, the nondominant upper extremity deep venous system is selected for the venous access. Rarely, the bilateral upper extremities will be thrombosed and venous access will be required in both arms. Again the goal is to gain access in a patent, peripheral vein to use for the CDT. The extent of thrombus is verified with venogram and/or IVUS.

Extreme caution must be taken when using a pharmacomechanical devices in the SVC due to risk of embolization of clot material to the pulmonary arteries and bradycardia. At the authors' institution, these devices are virtually never used in the SVC. The Angiojet device carries a black box warning for use in the SVC due to adenosine release from platelet lysis causing severe bradycardia. Thus in an effort to hasten the thrombolysis process, a bolus dose of tPA can be infused through the clot and then infusion catheters placed across the thrombosed portion of the SVC. All recommendations regarding dosing of tPA and heparin infusion from the previous sections are followed. The catheters and sheaths are secured to the skin and labeled. The patient is transferred to the intensive care unit.

## Immediate Post-procedural Patient Management

The post-thrombolysis procedural management follows the same course as for postprocedural DVT, PE, and IVC thrombolysis management.

## Procedural Course for SVC Lysis Check and Post-thrombolysis Patient Management

The patient is brought back to IR for the lysis check usually after 24 hours of thrombolytic infusion. Repeat venograms and IVUS can be performed to verify extent of residual thrombus. Suction thrombectomy can be used at this point to resolve further clot burden from the SVC and may decrease the risk of clot embolization to the pulmonary arteries (please see discussion regarding this technique in the pulmonary artery lysis section). Finally, careful balloon angioplasty may be performed to establish a patent channel for continued CDT. Infusion catheter(s) may need to be replaced and low-dose CDT continued for another 24 hours. CDT is typically successful within 48-72 hours unless the clot burden is more chronic or there is an underlying, uncorrected stenosis.

The stenosis is only able to be accurately visualized once the majority of clot burden is resolved. IVUS is particularly useful to delineate the point of maximal narrowing as well as provide luminal measurements for the SVC. It is the authors' opinion that a stent is often required in cases with SVC stenosis and thrombosis as relieving the stenosis with a permanent stent provides improved outflow into the right atrium thereby increasing the likelihood of CDT success and significantly decreasing the risk of recurrent occlusive thrombus. In contradistinction to adult SVC stenosis, pediatric SVC

stenosis is more often related to an indwelling central venous catheter rather than external compression from a thoracic tumor. There are particular considerations when choosing an SVC stent or a pediatric patient. First, more concern should be paid to the ability of the stent to precisely deploy across the stenosis and the ability of the stent to be sequentially dilated over time as the child grows, rather than the stent's radial force. The authors' preferred stent combination in pediatric cases in which the child is not fully grown is a self-expanding nitinol stent (such as a Zilver; Cook Medical, Bloomington, IN) constrained by a Palmaz balloon expandable stent (Cordis, Baar, Switzerland). The Palmaz stent can be loaded onto a balloon and dilated to a nominal size (ie, 6 or 8 mm) at its initial placement, and then periodically ballooned to a larger diameter as the patient grows. The initial Palmaz diameter chosen is based on the IVUS measurements obtained from nonstenotic portions of the SVC. The self-expanding, constrained nitinol stent diameter should be large enough for anticipated adult size SVC (12-18 mm), and eventually the Palmaz will be dilated to that size as well.

Once the clot burden has resolved and CDT is terminated, the patient is transitioned from heparin infusion to an anticoagulation medication which can be administered in the outpatient setting. The patient will need follow-up clinic appointments with the thrombosis clinic and IR. At the authors' institution, these patients are seen in clinic 1 month following the procedure. It is imperative these patients do not get lost to follow-up. Chest CT venogram is typically done every 6 months for the first year with subsequent IR clinic appointments to review the findings. There may be stent revisions or stent checks that need to be done within this time period. Finally, the patients will be scanned annually with contrast enhanced Chest CTs for a total of 3 years with IR clinic appointments to review the findings. If the patient has a stent, serial stent dilations will be coordinated as the pages ages to allow for dilation of the stent complex.

## Conclusion

In summary, there is very little available data demonstrating the efficacy of catheter directed venous thrombolysis in the pediatric population. Despite this, several IR and hematology teams are more commonly utilizing CDT with low-dose tPA infusions for pediatric patients to resolve acute venous thromboembolic disease. The current medical literature reports the risk of a major bleeding episode after pediatric endovascular thrombolysis is 0%-3%, and all bleeding rates appear to be decreasing in both the adult and pediatric populations due to stricter patient selection criteria as well as increased familiarity with dosing regimens of thrombolytic agents.[19,36] As these procedures become more common and trusted in the pediatric population, procedural standardization will be warranted, as the existing adult literature has shown high variability in procedural technique and subsequent outcomes. Clearly randomized clinical trials studying CDT in children with VTE disease are warranted. However, until trial data is available, it is evident that close collaboration between thrombosis experts in pediatric hematology, intensive care, and IR will allow pediatric specialists to provide the best patient care. Careful patient selection based on guidelines derived from adult thrombolysis studies is critical in the success of these cases.

## References


1. Raffini L, Huang YS, Witmer C, et al: Dramatic increase in venous thromboembolism in children's hospitals in the United States from 2001 to 2007. Pediatrics 124:1001-1008, 2009. https://doi.org/10.1542/peds.2009-0768
2. Andrew M, David M, Adams M, et al: Venous thromboembolic complications (VTE) in children: First analyses of the Canadian Registry of VTE. Blood 83:1251-1257, 1994
3. Monagle P, Chan AKC, Goldenberg NA, et al: Antithrombotic therapy in neonates and children. Chest 141(suppl 2):e737S-e801S, 2012. https://doi.org/10.1378/chest.11-2308
4. Boulet SL, Grosse SD, Thornburg CD, et al: Trends in venous thromboembolism-related hospitalizations, 1994-2009. Pediatrics 130:e812-e820, 2012. https://doi.org/10.1542/peds.2012-0267
5. Stein PD, Kayali F, Olson RE: Incidence of venous thromboembolism in infants and children: Data from the National Hospital Discharge Survey. J Pediatr 145:563-565, 2004. https://doi.org/10.1016/j.jpeds.2004.06.021
6. van Ommen CH, Heijboer H, Büller HR, et al: Venous thromboembolism in childhood: A prospective two-year registry in The Netherlands. J Pediatr 139:676-681, 2001. https://doi.org/10.1067/mpd.2001.118192
7. Jaffray J, Bauman M, Massicotte P: The impact of central venous catheters on pediatric venous thromboembolism. Front Pediatr 5. https://doi.org/10.3389/fped.2017.00005, 2017
8. Monagle P, Cuello CA, Augustine C, et al: American Society of Hematology 2018 Guidelines for management of venous thromboembolism: Treatment of pediatric venous thromboembolism. Blood Adv 2:3292-3316, 2018. https://doi.org/10.1182/bloodadvances.2018024786
9. Betensky M, Bittles MA, Colombani P, et al: How we manage pediatric deep venous thrombosis. Semin Interv Radiol 34:35-49, 2017. https://doi.org/10.1055/s-0036-1597762
10. Turpie AGG, Levine MN, Hirsh J, et al: Tissue plasminogen activator (rt-PA) vs heparin in deep vein thrombosis: Results of a randomized trial. Chest 97(suppl 4):172S-175S, 1990. https://doi.org/10.1378/chest.97.4_Supplement.172S
11. Enden T, Kløw NE, Sandvik L, et al: Catheter-directed thrombolysis vs anticoagulant therapy alone in deep vein thrombosis: Results of an open randomized, controlled trial reporting on short-term patency. J Thromb Haemost 7:1268-1275, 2009. https://doi.org/10.1111/j.1538-7836.2009.03464.x
12. Goldenberg NA, Durham JD, Knapp-Clevenger R, et al: A thrombolytic regimen for high-risk deep venous thrombosis may substantially reduce the risk of postthrombotic syndrome in children. Blood 110:45-53, 2007. https://doi.org/10.1182/blood-2006-12-061234
13. Goel R, Vedantham S, Goldenberg NA: Antithrombotic therapies: Anticoagulation and thrombolysis. Pediatr Clin North Am 60:1463-1474, 2013. https://doi.org/10.1016/j.pcl.2013.09.005
14. Vedantham S, Goldhaber SZ, Kahn SR, et al: Rationale and design of the ATTRACT study—A multicenter randomized trial to evaluate pharmacomechanical catheter-directed thrombolysis for the prevention of postthrombotic syndrome in patients with proximal deep vein thrombosis. Am Heart J 165:523-530.e3, 2013. https://doi.org/10.1016/j.ahj.2013.01.024
15. Vedantham S, Goldhaber SZ, Julian JA, et al: Pharmacomechanical catheter-directed thrombolysis for deep-vein thrombosis. N Engl J Med 377:2240-2252, 2017. https://doi.org/10.1056/NEJMoa1615066
16. Mewissen MW, Seabrook GR, Meissner MH, et al: Catheter-directed thrombolysis for lower extremity deep venous thrombosis: Report of a national multicenter registry. Radiology 211:39-49, 1999. https://doi.org/10.1148/radiology.211.1.r99ap4739
17. Wang CY, Ignjatovic V, Francis P, et al: Risk factors and clinical features of acute pulmonary embolism in children from the community. Thromb Res 138:86-90, 2016. https://doi.org/10.1016/j.thromres.2015.12.005

18. Kukreja K, Gruppo R, Chima R, et al: Developing a pediatric endovascular thrombolysis program: A single-center experience. Pediatr Radiol 43:1024-1029, 2013. https://doi.org/10.1007/s00247-013-2634-0
19. Greene LA, Goldenberg N: Deep vein thrombosis: Thrombolysis in the pediatric population. Semin Interv Radiol 29:36-43, 2012. https://doi.org/10.1055/s-0032-1302450
20. Gill AE, Ciszak T, Braun H, et al: Intravascular ultrasound versus digital subtraction angiography: Direct comparison of intraluminal diameter measurements in pediatric and adolescent imaging. Pediatr Radiol 47:450-457, 2017. https://doi.org/10.1007/s00247-016-3771-z
21. Mickley V, Schwagierek R, Schütz A, et al: Stent implantation after thrombectomy of pelvic veins. Indications, results. Zentralbl Chir 124:12-17, 1999
22. Albisetti M: Thrombolytic therapy in children. Thromb Res 118:95-105, 2006. https://doi.org/10.1016/j.thromres.2004.12.018
23. MacCartney C, Chan A: Thrombosis in children. Semin Thromb Hemost 37:763-761.
24. Zayed MA, De Silva GS, Ramaswamy RS, et al: Management of cavoatrial deep venous thrombosis: Incorporating new strategies. Semin Interv Radiol 34:25-34, 2017. https://doi.org/10.1055/s-0036-1597761
25. Zaidi AU, Hutchins KK, Rajpurkar M: Pulmonary embolism in children. Front Pediatr 5. https://doi.org/10.3389/fped.2017.00170, 2017
26. Brandão LR, Labarque V, Diab Y, et al: Pulmonary embolism in children. Semin Thromb Hemost 37:772-785, 2011. https://doi.org/10.1055/s-0031-1297168
27. Corrigan D, Prucnal C, Kabrhel C: Pulmonary embolism: The diagnosis, risk-stratification, treatment and disposition of emergency department patients. Clin Exp Emerg Med 3:117-125, 2016. https://doi.org/10.15441/ceem.16.146
28. Jiménez D, Aujesky D, Yusen RD: Risk stratification of normotensive patients with acute symptomatic pulmonary embolism. Br J Haematol 151:415-424, 2010. https://doi.org/10.1111/j.1365-2141.2010.08406.x
29. Massicotte MP, Dix D, Monagle P, et al: Central venous catheter related thrombosis in children: Analysis of the Canadian Registry of venous thromboembolic complications. J Pediatr 133:770-776, 1998. https://doi.org/10.1016/S0022-3476(98)70149-0
30. Kumar R, Kerlin BA: Thrombosis of the Abdominal Veins in childhood. Front Pediatr 5, 2017. https://doi.org/10.3389/fped.2017.00188
31. Tarango C, Kumar R, Patel M, et al: Inferior vena cava atresia predisposing to acute lower extremity deep vein thrombosis in children: A descriptive dual-center study. Pediatr Blood Cancer 65:e26785, 2018. https://doi.org/10.1002/pbc.26785
32. Ruggeri M, Tosetto A, Castaman G, et al: Congenital absence of the inferior vena cava: A rare risk factor for idiopathic deep-vein thrombosis. The Lancet 357:441, 2001. https://doi.org/10.1016/S0140-6736(00)04010-1
33. Häusler M, Hübner D, Delhaas T, et al: Long term complications of inferior vena cava thrombosis. Arch Dis Child 85:228-233, 2001. https://doi.org/10.1136/adc.85.3.228
34. Raffini L, Cahill AM, Hellinger J, et al: A prospective observational study of IVC filters in pediatric patients. Pediatr Blood Cancer 51:517-520, 2008. https://doi.org/10.1002/pbc.21622
35. Blevins EM, Glanz K, Huang YSV, et al: A multicenter cohort study of inferior vena cava filter use in children. Pediatr Blood Cancer 62:2089-2093, 2015. https://doi.org/10.1002/pbc.25662
36. Tarango C, Manco-Johnson MJ: Pediatric thrombolysis: a practical approach. Front Pediatr 5, 2017. https://doi.org/10.3389/fped.2017.00260
37. Eifler AC, Lewandowski RJ, Gupta R, et al: Optional or permanent: Clinical factors that optimize inferior vena cava filter utilization. J Vasc Interv Radiol 24:35-40, 2013. https://doi.org/10.1016/j.jvir.2012.09.021
38. Ye K, Qin J, Yin M, et al: Outcomes of pharmacomechanical catheter-directed thrombolysis for acute and subacute inferior vena cava thrombosis: A retrospective evaluation in a single institution. Eur J Vasc Endovasc Surg 54:504-512, 2017. https://doi.org/10.1016/j.ejvs.2017.06.025
39. Gupta V, Ambati SR, Pant P, et al: Superior vena cava syndrome in children. Indian J Hematol Blood Transfus 24:28-30, 2008. https://doi.org/10.1007/s12288-008-0020-0
40. Sessions KL, Anderson JH, Johnson JN, et al: AngioJet thrombolysis of SVC thrombosis after orthotopic heart transplantation: A case report. Pediatr Transplant 20:723-726, 2016. https://doi.org/10.1111/petr.12715
41. Rizvi AZ, Kalra M, Bjarnason H, et al: Benign superior vena cava syndrome: Stenting is now the first line of treatment. J Vasc Surg 47:372-380, 2008. https://doi.org/10.1016/j.jvs.2007.09.071