

**American College of Radiology  
ACR Appropriateness Criteria®**

**Clinical Condition:** Radiologic Management of Iliofemoral Venous Thrombosis

**Variant 1:** First episode of iliofemoral DVT. Symptoms present for <14 days, otherwise healthy.

Treatment/Procedure	Rating	Comments
Anticoagulation alone	5	
Catheter directed thrombolysis (CDT)	8	
Surgical thrombectomy	3	Perform this procedure if a contraindication to anticoagulation or thrombolytics exists.
<b><u>Rating Scale:</u></b> 1,2,3 Usually not appropriate; 4,5,6 May be appropriate; 7,8,9 Usually appropriate		

**Variant 2:** Iliofemoral DVT and symptoms  $\leq 10$  days. Computed tomography scan demonstrates potential for May-Thurner syndrome.

Treatment/Procedure	Rating	Comments
Anticoagulation alone	3	Perform this procedure if patient is not a candidate for thrombolysis.
Catheter directed thrombolysis (CDT) with evaluation and potential stent placement	8	
Surgical thrombectomy and repair of iliac vein	2	
<b><u>Rating Scale:</u></b> 1,2,3 Usually not appropriate; 4,5,6 May be appropriate; 7,8,9 Usually appropriate		

**Variant 3:** Iliofemoral DVT and limb-threatening ischemia (phlegmasia cerulea dolens).

Treatment/Procedure	Rating	Comments
Anticoagulation alone	3	
Catheter directed thrombolysis (CDT)	8	
Surgical thrombectomy	6	
<b><u>Rating Scale:</u></b> 1,2,3 Usually not appropriate; 4,5,6 May be appropriate; 7,8,9 Usually appropriate		

**Variant 4:** Iliofemoral DVT with minimal symptoms. DVT diagnosed one week ago.

Treatment/Procedure	Rating	Comments
Anticoagulation alone	7	Use of anticoagulation versus thrombolysis depends on general clinical condition of patient.
Catheter directed thrombolysis (CDT)	7	Use of anticoagulation versus thrombolysis depends on general clinical condition of patient. Perform this procedure in younger patients to avoid the risk of post-thrombotic syndrome.
Surgical thrombectomy	2	
Systemic thrombolysis	2	
<b><u>Rating Scale:</u></b> 1,2,3 Usually not appropriate; 4,5,6 May be appropriate; 7,8,9 Usually appropriate		

# RADIOLOGIC MANAGEMENT OF ILIOFEMORAL VENOUS THROMBOSIS

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## **Summary of Literature Review**

### **Introduction/Background**

Venous thromboembolism (VTE) consists of both deep vein thrombosis (DVT) and pulmonary embolism (PE) and is associated with significant morbidity. The incidence of VTE is approximately 100/100,000 population each year in the United States. The risk proportionately increases with age and ranges from 5/100,000 for people <15 years old to 500/100,000 for people >80 years old [1]. The major risk factors associated with VTE were described by Virchow: hypercoagulability, endothelial injury, and stasis. The most frequent risk factors include surgery, trauma, hip fracture, prolonged immobility, and several inherited and acquired hematological conditions [2]. Full-dose anticoagulation is the standard therapy for VTE, both for the acute and the long-term phase. The latest guidelines from the American College of Chest Physicians recommend treatment with a full dose of unfractionated heparin, low-molecular-weight-heparin, fondaparinux, vitamin K antagonist, or thrombolysis for most patients with objectively confirmed VTE [3]. Although anticoagulation effectively prevents thrombus extension, PE, death, and recurrence, many patients develop venous dysfunction resulting in post-thrombotic syndrome (PTS). This syndrome is characterized by pain, swelling, a heavy sensation, edema, pigmentation, and ulceration in severe cases [4]. The most severe PTS morbidity occurs in patients with iliofemoral DVT [5,6].

### **Initial Treatment of Acute DVT of the Lower Extremity**

Anticoagulation is the standard initial therapy for acute DVT. The main objective in the initial treatment of DVT is to prevent thrombus extension and recurrence. The evidence for the need for anticoagulation in patients with acute DVT is based on studies performed several years ago. The first trial comparing anticoagulation versus no anticoagulation in patients with VTE was published in 1960 [7]. This study showed that treatment with heparin and a vitamin K antagonist markedly reduced recurrent PE and mortality. Other studies have shown reduced mortality in patients when heparin is used to treat VTE compared to patients who did not receive anticoagulation [8,9]. In addition, a randomized controlled study reported a three-fold increase in the rate of recurrent VTE in patients treated with a vitamin K antagonist alone versus those initially treated with heparin and converted to a vitamin K antagonist [10]. In regards to duration of initial heparin therapy, 2 randomized clinical trials for patients with proximal DVT reported that intravenous unfractionated heparin administered for 5 to 7 days is as effective as 10 to 14 days, providing that it is followed by adequate long-term anticoagulant therapy [11,12]. This shorter duration of heparin therapy may also help reduce the incidence of heparin-induced thrombocytopenia. The currently recommended approach is to start both heparin and a vitamin K antagonist at the time of diagnosis and to discontinue heparin after 5 days, provided the international normalized ratio is  $\geq 2.0$  for at least 24 hours [3]. Multiple anticoagulation regimens are recommended to treat VTE and are beyond the scope of this document.

### **Early Thrombus Removal**

Although anticoagulation effectively prevents thrombus extension, PE, death, and recurrence, many patients develop venous dysfunction resulting in PTS. PTS occurs in 20%–50% of patients after acute DVT, and leg ulceration can occur in as many as 10% of patients [13,14]. PTS can lead to disability and reduced quality of life with important clinical and public health implications. Oral anticoagulation reduces thrombus propagation but does not effectively produce clot lysis, which can result in incomplete prevention of PTS. Patients with

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iliofemoral DVT are the subset of patients with the largest thrombus burden and the highest risk for post-thrombotic morbidity; up to 75% have chronic painful edema, and 40% have venous claudication when treated with anticoagulant therapy alone [3]. Treatments that actively remove thrombus have the potential to reduce the risk of developing PTS as well as relieve the immediate symptoms of DVT. The effectiveness of systemic thrombolysis to achieve early clot lysis has been investigated in a number of trials that found it to be associated with high rates of bleeding complications with relatively modest rates of thrombus clearance [15,16]. The rationale for catheter-directed thrombolysis (CDT) is that rapid lysis is achieved with lower doses of thrombolytic agent, resulting in fewer serious bleeding complications. In the National Venous Registry, patients treated with short-term DVT (<10 days) had better outcomes than those with older clots who underwent correction of underlying venous lesions after successful thrombolysis [17]. The addition of mechanical thrombus fragmentation during CDT is commonly used as part of the procedure. This is termed pharmacomechanical thrombolysis. Retrospective analyses comparing CDT alone versus pharmacomechanical thrombolysis suggest they are associated with similar rates of successful thrombolysis and major bleeding; however, pharmacomechanical thrombolysis was associated with shorter treatment times, shorter ICU/hospital stays, and reduced costs [18,19]. Furthermore, the CaVenT study was a prospective randomized controlled trial that evaluated the effects of additional CDT in patients with acute DVT in regards to PTS. This study demonstrated a clinically significant reduction of PTS after additional CDT was performed compared with conventional treatment alone [20].

### **Indications for Thrombolytic Therapy**

Although a definitive multicenter randomized controlled trial has yet to be completed, the available evidence favors use of CDT and pharmacomechanical thrombolysis in DVT patients with clinically severe manifestations of DVT. These severe manifestations include phlegmasia cerulea dolens (PCD), acute IVC thrombosis, and rapid thrombus extension despite anticoagulation as well as anatomically extensive DVT that includes the common femoral and/or iliac vein since this degree of thrombus carries a higher risk of recurrent DVT and PTS [21].

### **Acute Iliofemoral Deep Vein Thrombosis**

Recommendations for early thrombus removal are based on balancing the benefits of preventing PTS versus the risks of therapy (eg, bleeding, recurrent DVT). A recent meta-analysis evaluating treatment options for iliofemoral DVT revealed a statistically significant reduction in the risk of PTS and venous obstruction in patients treated with CDT versus those treated with anticoagulation alone [22]. The Society for Vascular Surgery (SVS) and the American Venous Forum (AVF) have also recently published joint clinical practice guidelines for early thrombus removal in patients with acute iliofemoral DVT [23]. They recommend early thrombus removal in patients who present with acute iliofemoral DVT, symptoms <14 days, low risk of bleeding, and a reasonable life expectancy. The 14 day cut off is somewhat arbitrary, however among the patients enrolled in the National Venous Registry, patients with DVT and symptoms >10 days had significantly worse outcomes than patients with symptoms <10 days. Other guidelines have suggested that DVT associated with symptoms  $\leq$ 14 days should be considered acute [24], and a recently published randomized trial included patients with symptoms <21 days [25].

### **Phlegmasia Cerulea Dolens**

PCD is characterized by massive swelling, cyanosis, and pain resulting from extensive thrombosis of the iliofemoral venous system [26]. Venous gangrene occurs when extensive thrombus leads to venous hypertension and small arterial collapse due to the surrounding tissue pressure. Calf compartment pressures of  $\geq$ 50 mm Hg have been documented in association with PCD [27]. Since this is a potentially life- and limb-threatening condition, the benefits of early thrombus removal outweigh the risks in this clinical scenario.

### **May-Thurner Syndrome**

May-Thurner syndrome is characterized by compression of the left common iliac vein between the right common iliac artery and vertebrae. This compression is thought to induce endothelial irritation and lead to left lower extremity DVT. The importance of underlying iliac vein lesions cannot be fully appreciated in patients treated with anticoagulation alone. As early thrombus removal techniques have advanced, it has become clear that underlying iliac vein lesions, in this case compression, may contribute to many cases of iliofemoral DVT. In the National Venous Registry, 33% of limbs required treatment with stents, and the 1-year patency (74%) was significantly better in those limbs compared to the limbs without stent placement (53%;  $P<.001$ ) [17].

## Pharmacomechanical Thrombolysis Devices

There are 2 most commonly used devices for pharmacomechanical thrombolysis. The first is a device that uses high-velocity saline jets for the percutaneous break-up and removal of thrombus. This device also has a “power pulse” function allowing additional thrombolytic penetration into the thrombus. The second device utilizes a macerating wire to break up the thrombus while thrombolytic. It consists of a catheter for infusion of fluids into a treatment area isolated between 2 occluding balloons. These devices are currently incorporated in the ATTRACT study (Acute Venous Thrombus Removal with Adjunctive Catheter-Directed Thrombolysis), which is a randomized controlled trial evaluating subsequent PTS in patients with acute DVT treated with pharmacomechanical thrombolysis plus standard anticoagulation versus anticoagulation alone in the treatment of acute DVT [28].

## Surgical Thrombectomy

Venous thrombectomy has been compared with anticoagulation in the past and has been demonstrated to potentially preserve the venous function. One meta-analysis comparing the efficacy of anticoagulation, surgical thrombectomy, and CDT was recently published and found that both surgical thrombectomy and CDT decrease the incidence of PTS [22]. The SVS/AVF guidelines recommend surgical venous thrombectomy in patients who are candidates for anticoagulation but in whom thrombolytic therapy is contraindicated. For patients who are candidates for either approach, a higher value is placed on avoiding the more invasive procedure and the potential surgical complications [23].

## Patient Selection

Patient selection for CDT is individualized. Important considerations include the patient’s bleeding risk profile, life expectancy, anticipated activity level, and their willingness to undergo a procedure that may require an overnight hospital stay. Successful thrombolysis is most likely achieved in patients with recently formed thrombus and symptom duration less than 10–14 days [17]. Patients who have short life expectancy, do not ambulate, have had recent surgery or trauma, have intracranial lesions, and have thrombocytopenia are poor candidates [21].

## Compression Stockings

The role of compression stockings in the management of chronic venous disorders has been well established [29]. Compression stockings improve the calf muscle pump function and reduce edema. The use of graded elastic compression stockings decreases by 50% the incidence of objectively defined PTS after a first episode of proximal DVT treated with conventional anticoagulation. For this reason, the SVS/AVF guidelines recommend 30-40 mm Hg compression stockings for 2 years following early thrombus removal [23].

## Summary

- VTE is associated with significant morbidity.
- The main objectives of anticoagulation are to prevent thrombus extension and early and late recurrence of VTE.
- Conventional anticoagulation alone does not prevent post-thrombotic syndrome.
- Catheter-directed thrombolysis and pharmacomechanical thrombolysis may decrease the incidence in PTS in patients with acute iliofemoral DVT with proper patient selection.
- The ATTRACT trial is a randomized controlled trial currently underway and will likely provide further evidence regarding the clinical utility of pharmacomechanical thrombolysis for patients with acute iliofemoral DVT.

## Supporting Documents

- [ACR Appropriateness Criteria® Overview](#)
- [Evidence Table](#)

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The ACR Committee on Appropriateness Criteria and its expert panels have developed criteria for determining appropriate imaging examinations for diagnosis and treatment of specified medical condition(s). These criteria are intended to guide radiologists, radiation oncologists and referring physicians in making decisions regarding radiologic imaging and treatment. Generally, the complexity and severity of a patient's clinical condition should dictate the selection of appropriate imaging procedures or treatments. Only those examinations generally used for evaluation of the patient's condition are ranked. Other imaging studies necessary to evaluate other co-existent diseases or other medical consequences of this condition are not considered in this document. The availability of equipment or personnel may influence the selection of appropriate imaging procedures or treatments. Imaging techniques classified as investigational by the FDA have not been considered in developing these criteria; however, study of new equipment and applications should be encouraged. The ultimate decision regarding the appropriateness of any specific radiologic examination or treatment must be made by the referring physician and radiologist in light of all the circumstances presented in an individual examination.