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Role of Catheter-directed Thrombolysis in Management of Iliofemoral Deep Venous Thrombosis[1]

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Abbreviations: CDT = catheter-directed thrombolysis, DVT = deep venous thrombosis, IVC = inferior vena cava, PTS = postthrombotic syndrome

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See discussion on this article by Zvavanjanja and Cohen (pp 1576–1578).

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SA-CME LEARNING OBJECTIVES

After completing this journal-based SA-CME activity, participants will be able to:

- Describe the patient- and disease-specific factors to consider before performing endovascular DVT intervention.
- List the categories of currently used endovascular thrombolysis and thrombectomy modalities.
- Summarize key points from the current evidence on endovascular DVT therapy.

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The treatment for iliofemoral deep venous thrombosis (DVT) is challenging, as the use of anticoagulation alone can be insufficient for restoring venous patency and thus lead to prolongation of acute symptoms and an increased risk of chronic complications, including venous insufficiency and postthrombotic syndrome (PTS). In these cases, earlier and more complete thrombus removal can ameliorate acute symptoms and reduce long-term sequelae. Endovascular therapies involving the use of pharmacologic, mechanical, and combined pharmacomechanical modalities have been developed to achieve these goals. The most frequently used of these techniques, catheter-directed thrombolysis (CDT), involves the infusion of a thrombolytic agent through a multiple–side-hole catheter placed within the thrombosed vein to achieve high local doses and thereby break down the clot while minimizing systemic thrombolytic agent exposure. Randomized controlled trial results have indicated decreased PTS rates and improved venous patency rates in patients treated with CDT compared with these rates in patients treated with anticoagulation. The use of newer pharmacomechanical techniques, as compared with conventional CDT, reduces procedural times and thrombolytic agent doses and is the subject of ongoing investigations. Endovascular thrombus removal techniques offer a means to improve venous valvular function and decrease the risk of debilitating long-term complications such as PTS and are a promising option for treating patients with iliofemoral DVT.

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Introduction

The treatment of patients with iliofemoral lower-extremity deep venous thrombosis (DVT) involving the iliac, femoral, and popliteal veins remains challenging. Morbidity resulting from short- and long-term complications contributes to substantial patient debility and health care costs, the implications of which are compounded by projections of increased incidences of venous thromboembolism, including DVT, in the coming decades (1). In the acute setting, DVT is aimed at restoring venous patency, preventing thrombus extension, and reducing the incidence of pulmonary embolism. Long-term therapeutic goals include minimizing the incidence of recurrent thrombosis and decreasing the risk of chronic venous insufficiency and postthrombotic syndrome (PTS). The current standard of care is systemic anticoagulation, which can prevent thrombus propagation; with this procedure, however, endogenous fibrinolysis is required for clot dissolution. Consequently, larger-volume clots, particularly iliofemoral DVTs, are a therapeutic challenge, as anticoagulation often fails to restore venous patency and thus predisposes the patient to recurrent thrombosis and chronic complications due to associated venous valvular disruption. Adjunctive treatments with external compressive devices such as graded-compression stockings also have

TEACHING POINTS

- Larger-volume clots, particularly iliofemoral DVTs, are a therapeutic challenge, as anticoagulation often fails to restore venous patency and thus predisposes the patient to recurrent thrombosis and chronic complications due to associated venous valvular disruption.
- Endovascular intervention for acute or subacute DVT is well accepted, given the relatively high likelihood of restored venous patency; however, for chronic DVT, it is reserved for severely symptomatic patients owing to difficulties in recanalizing chronically thrombosed veins.
- Limitations of the described therapies have fueled the development of a variety of endovascular thrombus removal techniques, which can be categorized into pharmacologic, mechanical, and combined (pharmacomechanical) groups.
- Periprocedural complications vary among modalities and patient selection criteria but are generally comparable between pharmacomechanical CDT and traditional CDT techniques. The most feared major complications—intracranial hemorrhage, symptomatic pulmonary embolism, and death—have been found to be exceedingly rare, reportedly occurring in 0%–4% of cases involving CDT treatment.
- The Society of Interventional Radiology, Society for Vascular Surgery, and American Heart Association have established concordant guidelines that support the use of CDT and pharmacomechanical CDT for acute iliofemoral DVT in recently ambulatory patients with good functional status.

been shown to be ineffective for preventing PTS (2); these results highlight the need to perform more effective early intervention before irreversible venous damage occurs. These limitations have prompted the development of endovascular thrombus removal and dissolution strategies, including catheter-directed thrombolysis (CDT), pharmacomechanical CDT, and percutaneous mechanical thrombectomy. The indications for and effectiveness of these techniques remain subjects of investigation; however, there is increasing evidence supporting the use of these modalities for the treatment of patients with proximal DVT in appropriately selected cases.

Clinical Evaluation

In only a minority of DVT cases is the clot burden severe enough to threaten limb viability and necessitate urgent endovascular thrombus clearance for limb preservation. For the majority of patients, treatment is initiated on a nonurgent basis for nonthreatened limbs to provide symptom relief and prevent long-term complications. Given the inherent procedural complications associated with endovascular interventions, detailed preprocedural clinical evaluation and consideration of the risk-to-benefit ratio are merited.

Disease-specific factors to consider include duration of symptomatic disease, location of DVT extension, and underlying anatomic abnormality. The chronicity of DVT symptoms is divided into acute (≤14 days), subacute (15–28 days), and chronic (>28 days) categories. Endovascular intervention for acute or subacute DVT is well accepted, given the relatively high likelihood of restored venous patency; however, for chronic DVT, it is reserved for severely symptomatic patients owing to difficulties in recanalizing chronically thrombosed veins. The locations of DVTs are stratified into proximal regions, encompassing the iliac, femoral, and popliteal veins; and distal regions, encompassing the calf veins. Whereas distal DVT most often has a benign disease course, proximal DVT is much more strongly associated with acute pulmonary embolism and chronic symptoms such as PTS (seen in 30%–75% of cases), severe limb edema, pain, and skin ulceration (3,4) (Fig 1). Iliofemoral DVT is associated with a particularly high risk of pulmonary embolism and PTS; therefore, patients with this condition are excellent candidates for adjunctive endovascular therapy.

Patient-specific factors also merit consideration when determining the appropriateness of endovascular intervention. Patients who are chronically nonambulatory are unlikely to experience clinically meaningful improvement, and those with bleeding disorders are at an unacceptably high risk of developing hemorrhagic complications. Endovascular thrombolysis is contraindicated for patients with active internal bleeding, a history of a recent cerebrovascular event, or other absolute contraindications to anticoagulation. Conversely, younger, healthier, and recently ambulatory patients stand to benefit from more aggressive therapy—even in cases of chronic DVT. Also, younger patients, as compared with older and/or debilitated patients, can generally tolerate higher doses of anticoagulants and thrombolytic agents without complications (5). The presence of indwelling venous devices such as inferior vena cava (IVC) filters (Fig 2) also places patients at an increased risk of developing DVT (6).

Imaging

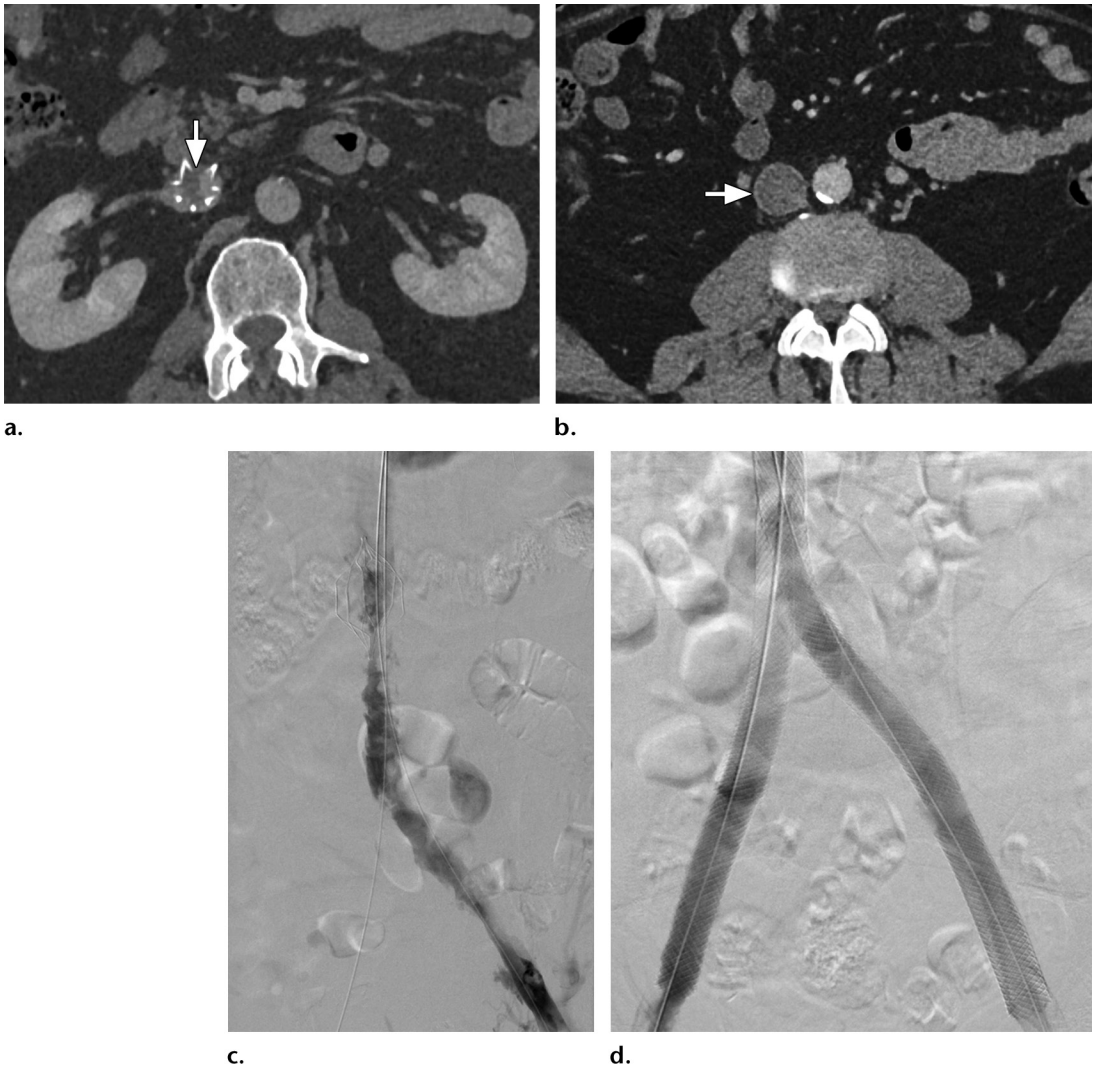
Lower-extremity duplex ultrasonography (US) is the examination most commonly used to exclude DVT and can be sufficient for preprocedural imaging in young healthy patients with provoked DVT. However, US enables limited evaluation of vessels above the inguinal ligaments, including the iliac veins and IVC, which can harbor thrombi or anomalies that necessitate additional intervention. In patients with nonprovoked DVT, chronic DVT, DVT in the setting of a probable anatomic abnormality, or an indwelling IVC filter (Fig 2), more detailed evaluation with CT or magnetic resonance (MR) venography



Figure 1. Subacute left iliofemoral DVT in a 62-year-old woman with an underlying malignancy. **(a)** Photograph of the left leg at presentation shows extensive skin changes related to venous stasis, including erythema and ulceration. **(b)** Initially obtained prone unsubtracted angiogram shows extensive multifocal occlusive filling defects, corresponding to the thrombus, throughout the left iliofemoral veins. Venous access was obtained via the left popliteal vein. A Berenstein catheter (Cook Medical, Bloomington, Ind) (arrows) was advanced to the level of the left common iliac vein. **(c)** Prone digital subtraction angiogram obtained after CDT shows residual thrombus in the left common and external iliac veins. **(d)** Fluoroscopic image shows a percutaneous thrombectomy device (Arrow-Trerotola Percutaneous Thrombectomy Device; Teleflex, Morrisville, NC) deployed within the left common iliac vein. Subsequent thrombectomy also was performed by using a pharmacomechanical peripheral thrombectomy device (AngioJet Rheolytic Thrombectomy System; Boston Scientific, Marlborough, Mass) (not shown). **(e)** Digital subtraction angiogram obtained after the placement of a Wallstent (Boston Scientific), which spans the left common and left external iliac veins, shows restoration of venous flow. Arrows mark the ends of the stent. **(f)** Photograph of the legs 10 months after pharmacomechanical thrombolysis and stent placement shows resolution of the initial cutaneous findings.

(Figs 3b, 4a) is recommended. Some authors have advocated the use of cross-sectional imaging evaluation for all patients who will possibly undergo endovascular intervention (7)—to more accurately assess the location and extent of DVT, exclude underlying structural lesions, and determine the optimal venous access site. Thrombus extension or free-floating thrombus in the IVC is a critical finding because if either is identified, IVC filter placement before the endovascular thrombolysis or thrombectomy procedure will be required to prevent periprocedural pulmonary

Figure 2. IVC filter–related chronic DVT, which caused debilitating lower-extremity swelling, in a 49-year-old man. **(a)** Axial computed tomographic (CT) venogram shows a nonoccclusive thrombus (arrow) within the infrarenal IVC filter basket (TrapEase; Cordis, Bridgewater, NJ). **(b)** Axial CT venogram shows thrombus extension to the infrarenal IVC (arrow), where it is occlusive. **(c)** Bilateral popliteal venous access was obtained, and wire and catheter systems were used to cross the thrombus within the IVC. Subtraction cavagram obtained after initial pharmacomechanical peripheral thrombectomy was performed by using the AngioJet device shows residual thrombus and multifocal stenosis throughout the IVC and left common iliac vein. **(d)** After thrombectomy was performed by using the AngioJet device, balloon angioplasty was used to deploy a Wallstent over the IVC filter. Overlapping stents were then deployed through the infrarenal IVC and bilateral iliac veins. Subsequently obtained subtraction angiogram shows no intrastent filling defects.



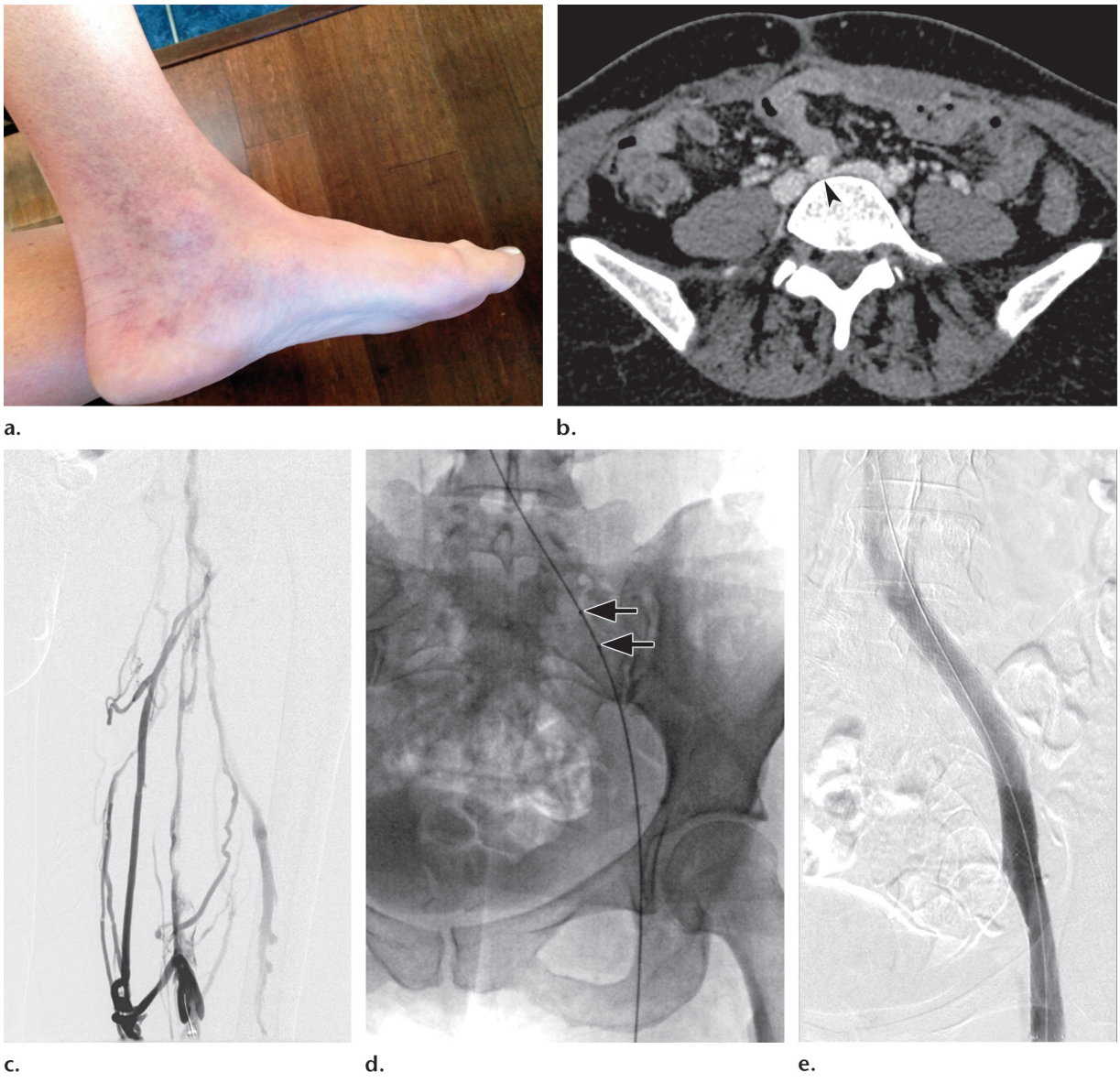
embolism. Notable anatomic risk factors include iliac venous stenosis in May-Thurner syndrome (Fig 3) (8), with which the underlying narrowing must be addressed to prevent recurrent DVT. Duplication of the IVC (Fig 4) (9) is another anomaly to exclude, as thrombus and associated caval stenosis can occur in both caval lumina.

CT venography has several advantages over duplex US, as mentioned earlier, including the benefit that it can be combined with CT pulmonary angiography for simultaneous exclusion of pulmonary embolism. CT venography facilitates more detailed anatomic evaluation of the proximal veins above the inguinal ligament and thus can be used to detect iliac DVT that is occult on US images (10,11). Disadvantages include radiation exposure and contrast material load in patients with renal insufficiency.

MR venography can facilitate anatomic evaluation similar to that possible with CT venography and has the added benefits of enabling superior evaluation near regions of osseous structures that can be obscured by artifact on CT images and providing the option to perform non–contrast material–enhanced evaluation. However, acquisition times can be substantially longer, and patients with non–MR imaging–compatible implants such as certain cardiac pacer and

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Figure 3. Chronic left iliofemoral DVT in a 35-year-old woman with May-Thurner syndrome. **(a)** Photograph of the left ankle at presentation shows cutaneous findings related to extensive DVT, which was caused by venous hypertension. **(b)** Axial contrast material–enhanced CT image shows narrowing of the proximal left common iliac vein (arrowhead) due to compression from the overlying right common iliac artery. **(c)** Digital subtraction angiogram obtained after left popliteal venous access shows extensive filling defects, corresponding to the thrombus, throughout the left femoral vein. **(d)** With fluoroscopic guidance, an AngioJet rheolytic thrombectomy device was advanced over a wire to the left common iliac vein for clot removal. Arrows point to the tip markers on the stent. **(e)** Prone digital subtraction angiogram obtained after thrombectomy with the AngioJet device and placement of overlapping Wallstent and Zilver (Cook Medical) stents shows no residual stenoses or filling defects.



automatic implantable cardioverter defibrillator devices, stents, and IVC filters cannot undergo MR venography.

Treatment Modalities

Systemic Anticoagulation

Systemic anticoagulation, which targets thrombus propagation, is the standard of care for patients with DVT owing to its favorable safety profile and clinicians' extensive clinical experience with this intervention. Treatment is initiated in the acute setting and typically continued for at least 6 months following the diagnosis of DVT. Traditional therapy has involved the use of low-molecular-weight heparin bridged to warfarin, but new anticoagulants such as factor Xa (eg, apixaban and rivaroxaban) and direct thrombin inhibitors (eg, dabigatran) are effective for acute and chronic applications (12). The major limitation of anticoagulation as an isolated therapy for acute DVT is its lack of a thrombolytic effect, which limits the speed and extent of venous recanalization for large clots and, in turn, leads to prolongation of acute symptoms, more severe venous valvular damage,

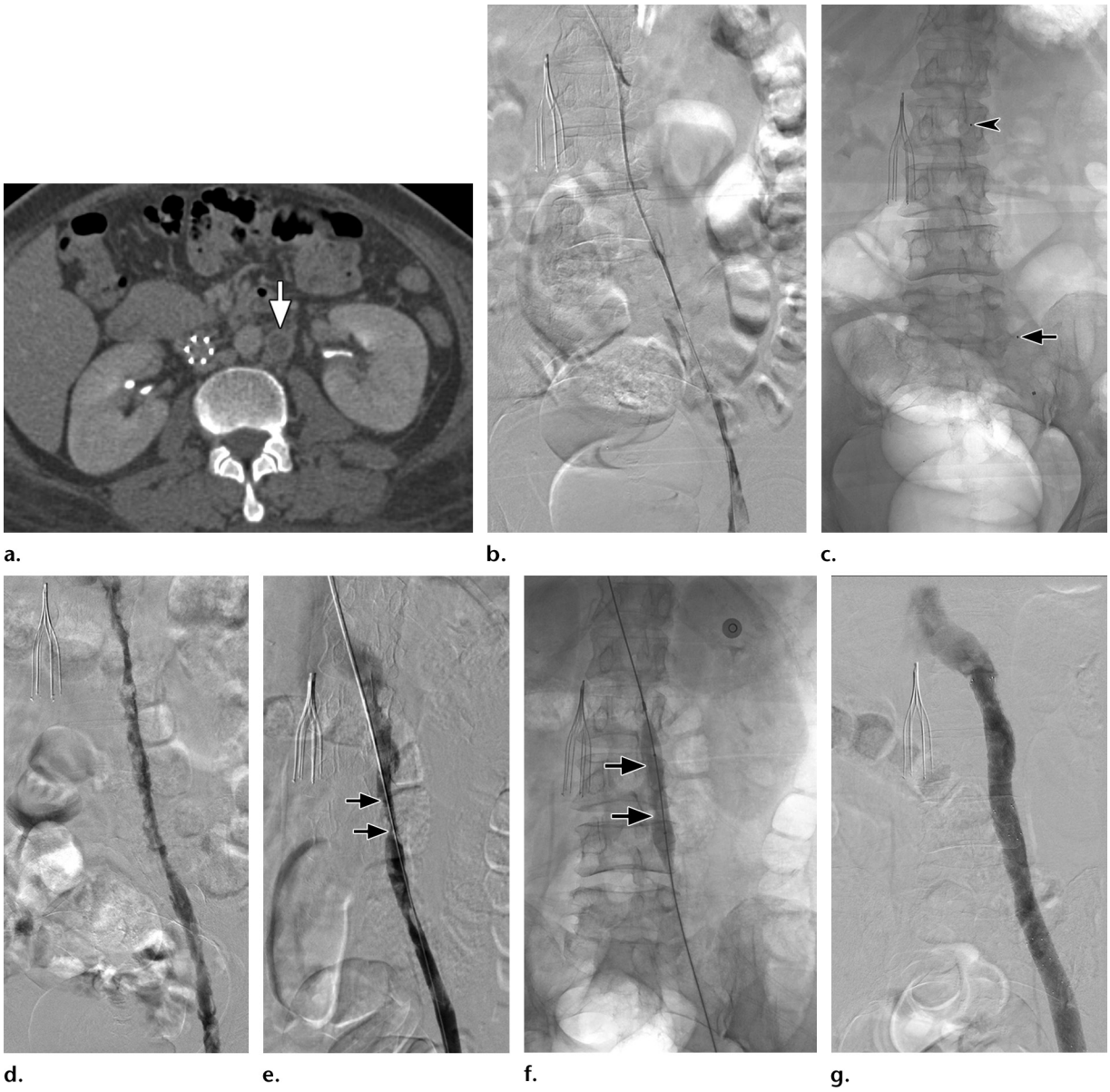


Figure 4. Subacute DVT in a 64-year-old woman with a duplicated IVC. **(a)** Axial CT venogram shows a duplicated IVC with a thrombus (arrow) in the left IVC and a previously placed filter in the right IVC. **(b)** Initially obtained subtracted venogram shows an extensive clot throughout the left IVC and left iliac vein; these findings correlate with the CT findings. **(c)** A multiple–side-hole infusion catheter was placed in the IVC and positioned by using a distal tip marker (arrowhead) at the level of the left renal vein and a proximal tip marker (arrow) at the level of the left common iliac vein. **(d)** Subtracted venogram obtained after 48 hours of CDT shows a residual clot throughout the left IVC. **(e)** Subsequently obtained subtracted venogram shows short-segment stenosis (arrows) of the left infrarenal IVC. **(f)** Angioplasty was performed by using a 12-mm balloon to address the stenosis (arrows). **(g)** Overlapping 14-mm Zilver stents were placed in the left IVC. Venogram obtained after the stent placement shows a patent left IVC, with no residual intraluminal thrombus.

and a higher risk for long-term complications, particularly in cases of iliofemoral DVT. The effectiveness of new anticoagulants for the reduction of large DVTs is not fully elucidated, as patients requiring endovascular therapy—the population at highest risk for insufficient thrombus removal—have been excluded in randomized controlled trials of these agents. A study of new anticoagulants used with endovascular therapy and continued for at least 6 months revealed a low (5.5%) rate and mild severity of PTS at a mean follow-up period of 22 months (13).

Systemic Thrombolysis

Systemic thrombolysis, as compared with anticoagulation, facilitates improved thrombus clearance. However, it is no longer in clinical use, as the results of several randomized controlled trials have indicated that this procedure is associated with a substantially (~10%) increased risk of bleeding complications and no decreased risk of PTS (14).

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Catheter-directed Thrombolysis

Limitations of the described therapies have fueled the development of a variety of endovascular thrombus removal techniques, which can be categorized into pharmacologic, mechanical, and combined (pharmacomechanical) groups. The pharmacologic and combined approaches are the most commonly used, with isolated percutaneous mechanical thrombectomy reserved for the minority of patients in whom the use of thrombolytic agents is contraindicated.

CDT, a pharmacologic thrombus removal approach, is the most commonly used overall and involves the delivery of the thrombolytic agent through a multiple–side-hole infusion catheter positioned within the thrombosed vein. This technique enables higher local drug concentrations than does systemic thrombolytic agent administration while lowering the systemic dose, as well as reduced exposure of tissue plasminogen activator to circulating inhibitors, and it protects plasmin from neutralization by α_2-antiplasmin. Commonly used thrombolytic agents include recombinant tissue plasminogen activator (eg, alteplase), streptokinase, and urokinase. The standard dosage regimen for tissue plasminogen activator infusion is 0.01 (mg · kg^{-1})/h (15) infused for 1–4 days (mean infusion time, 55.2 hours [16]). After CDT, venography should be performed to evaluate the extent of residual thrombus and exclude any underlying structural abnormalities that are contributing to DVT formation. Residual clots can be addressed with balloon maceration, mechanical thrombectomy, and/or further CDT. Venoplasty and stent placement can be used to address short-segment venous stenoses.

The advantages of using CDT, as compared with using anticoagulation alone, include improved thrombus reduction and reduced rates of PTS following iliofemoral DVT, as evidenced in several randomized controlled trials (Tables 1 and 2) (17–21). Results of the CaVenT (Catheter-directed Venous Thrombolysis in Acute Iliofemoral Vein Thrombosis) trial, which were derived by using the validated Villalta PTS scale, indicated an 11.5% reduction in PTS rate in patients treated with CDT compared with the PTS rate in those treated with anticoagulation (41% vs 56%, $P = .047$) (15,18,22) at 24-month follow-up. In the TORPEDO (Thrombus Obliteration by Rapid Percutaneous Endovenous Intervention in Deep Venous Occlusion) trial, a single-center randomized controlled trial of acute symptomatic proximal DVT, results obtained by using a nonvalidated PTS symptoms scale indicated a 22.8% lower rate of PTS in patients treated with endovenous intervention versus anticoagulation (7% vs 30%, $P < .001$) (19) at a mean follow-up period of 30 months. The variations in PTS reduction are possibly related to differences in treatment technique and modality, as well as variations in the way clinical outcomes were measured and reported. Treatment with CDT has also led to significantly improved rates of venous patency, as evidenced in the CaVenT trial, in which there was an 18.9% higher 6-month iliofemoral venous patency rate in the CDT versus control anticoagulation treatment group (66% vs 47%, $P = .012$) (18). Chronic venous occlusion and reflux have been associated with lower quality of life scores (23); this finding suggests an association between improved venous patency rates and decreased symptoms. The degree of venous valvular preservation after CDT was evaluated in a study involving patients with acute proximal DVT: Intact venous valves were seen at venography in 83% of cases at a mean follow-up period of 3.5 years (24). It is notable that despite favorable venous patency and valvular preservation results, the rates of recurrent venous thromboembolism varied substantially between studies (Table 2).

The incidences of complications related to CDT are modest, and these complications are primarily due to hemorrhage, with major hemorrhage occurring in up to 2% of cases (15,17,18,21,22). Bleeding complications occur most often at the venous access site and are more likely to occur with multiple access attempts; the majority of these cases do not result in permanent sequelae. The overall safety profile of current CDT procedures is improved compared with the safety reported in earlier CDT studies (25) and reflective of improvements in technique and technology.

A major disadvantage of CDT is the long infusion time, during which intensive care monitoring is required, taxing patients and health care resources. Strategies to overcome this limitation include pharmacomechanical CDT, in which mechanical thrombus removal is combined with CDT, and US-assisted CDT. US-assisted CDT involves the use of an ultrasound-emitting catheter system to accelerate thrombolysis by disaggregating fibrin and improving drug penetration (26,27). Despite their promising in vitro results, clinical studies have failed to reveal a benefit to using the more expensive US-assisted CDT rather than conventional CDT. In the BERNUTIFUL (BERN Ultrasound-enhanced Thrombolysis for Ilio-Femoral Deep Vein Thrombosis versus Standard Catheter Directed Thrombolysis) trial, when CDT was compared with US-assisted CDT for treatment of patients with acute iliofemoral DVT, no statistically significant

Table 1: Results from Randomized Controlled Trials of CDT and Pharmacomechanical CDT

Study and Treatment Group*	No. of Patients	Complete Resolution†	Partial Resolution†	Major Bleeding†	Minor Bleeding†	Pulmonary Embolism†	Death†
Elsharawy and Elzayat, 2002 (17)							
Anticoagulation	17	2 (12)	8 (47)	0	0	1 (6)	0
CDT	18	5 (28)	5 (28)	0	0	0	0
Enden et al (CaVenT study), 2012 (18)							
Anticoagulation	99	NA	NA	0	0	0	0
CDT	90	43 (47)	37 (41)	3 (3)	5 (6)	0	0
Sharifi et al (TORPEDO study), 2012 (19)							
Anticoagulation	92	NA	NA	NA	NA	7 (8)	4 (4)
PEVI	91	NA	NA	NA	NA	1 (1)	1 (1)
Cakir et al, 2014 (20)							
Anticoagulation	21	1 (5)	15 (71)	NA	NA	4 (19)	NA
PAT	21	12 (57)	8 (38)	NA	NA	1 (5)	NA
Engelberger et al (BERNUTIFUL study), 2015 (21)							
CDT	24	NA	NA	0	2 (8)	NA	NA
US-assisted CDT	24	NA	NA	1 (4)	3 (13)	NA	NA

*Numbers in parentheses are corresponding reference numbers. NA = not available, PAT = percutaneous aspiration thrombectomy, PEVI = percutaneous endovenous intervention.
†Data are numbers of patients, with percentages based on the number of patients in parentheses.

difference in PTS symptoms or thrombus load reduction was found between the two treatment groups (21). These findings correlated with the results of an earlier retrospective study (28).

Pharmacomechanical CDT and Percutaneous Mechanical Thrombectomy

Pharmacomechanical CDT and combined percutaneous mechanical thrombectomy and CDT have been used to accelerate thrombolysis and decrease the required drug dose, compared with these parameters for conventional CDT. The "power-pulse" technique involves the use of the AngioJet Rheolytic Thrombectomy System (Fig 3d), which deploys a high-pressure fluid jet to create negative pressure gradients (Bernoulli-Venturi effect) and thereby draw the thrombus into the catheter, where it is fragmented and aspirated. With the "buzz and lyse" variant of this technique, diluted thrombolytic agent (ie, 15–25 mg of tissue plasminogen activator diluted into 250 mL of saline solution) is pulse sprayed without aspiration, and after a 30–45-minute dwell time, thrombus aspiration is performed. In larger vessels such as the iliac veins and IVC, curved guide catheters can be used to facilitate adequate surface contact of the AngioJet catheter with the vessel wall, which is essential to achieving optimal results. Another pharmacomechanical CDT technique, isolated thrombolysis, involves the use of the Trellis peripheral infusion system (Covidien, Mansfield, Mass), whereby an oscillating wire is used to circulate thrombolytic agent between proximal and distal occlusion balloons (29). The movement of the wire macerates the thrombus and mixes the thrombolytic drug within the thrombus, after which the proximal balloon is deflated to allow thrombus aspiration. It should be noted that the Trellis system is currently off the market because of a mass recall initiated in December 2014. Other mechanical thrombectomy instruments such as the Arrow-Trerotola Percutaneous Thrombectomy device (Fig 1d), which consists of a rotational mechanism, have been used in conjunction with CDT or as instruments for isolated percutaneous mechanical thrombectomy (30).

Periprocedural complications vary among modalities and patient selection criteria but are generally comparable between pharmacomechanical CDT and traditional CDT techniques. The most feared major complications—intracranial hemorrhage, symptomatic pulmonary embolism, and death—have been found to be exceedingly rare, reportedly occurring in 0%–4% of cases involving CDT treatment (17,18,21,31). The most prevalent complication is major hemorrhage, which, according to a comprehensive review of available stud-

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Table 2: Long-term Outcomes in Randomized Controlled Trials of CDT and Pharmacomechanical CDT

Study*	Outcome	Treatment Group†	*P* Value
Elsharawy and Elzayat, 2002 (17)	Complete iliofemoral venous patency at 6 months	Anticoagulation: 2 (12%) CDT: 13 (72%)	<.001
	Venous reflux at 6 months	Anticoagulation: 7 (41%) CDT: 2 (11%)	.042
Enden et al (CaVenT study), 2012 (18)	Complete iliofemoral venous patency at 6 months	Anticoagulation: 45 (47%) CDT: 58 (66%)	.012
	PTS at 24 months	Anticoagulation: 55 (56%) CDT: 37 (41%)	.047
	Recurrent venous thromboembolism at 24 months	Anticoagulation: 18 (18%) CDT: 10 (11%)	>.05
Sharifi et al (TORPEDO study), 2012 (19)	PTS at mean follow-up of 30 months	Anticoagulation: 24 (30%) PEVI: 6 (7%)	<.001
	Recurrent venous thromboembolism at mean follow-up of 30 months	Anticoagulation: 13 (16%) PEVI: 4 (5%)	.02
Cakir et al, 2014 (20)	Complete venous patency at 12 months	Anticoagulation: 1 (5%) PAT: 12 (57%)	<.001
	Mean clinical symptom score at 12 months‡	Anticoagulation: 2.4 PAT: 0.81	<.001
Engelberger et al (BERNUTIFUL study), 2015 (21)	Mean percentage reduction in thrombus load from the baseline at 15 hours of CDT§	CDT: 54% US-assisted CDT: 55%	.91
	Mean hospital stay	CDT: 2.8 days US-assisted CDT: 2.7 days	.83
	Mean Villalta scale–based clinical symptom score at 3 months	CDT: 1.9 US-assisted CDT: 3.0	.21

*Numbers in parentheses are corresponding reference numbers.
†Unless otherwise indicated, data are numbers of patients, with percentages in parentheses. PAT = percutaneous aspiration thrombectomy, PEVI = percutaneous endovenous intervention.
‡Scores are based on a nonvalidated symptom score system involving a scale of 0 (indicating the fewest symptoms) to 6 (indicating the most symptoms).
§Data were calculated by using US-based length-adjusted thrombus scores.

ies provided in a recent Society of Interventional Radiology consensus statement, is seen in 2.8% of cases involving CDT (5). Bleeding complications can be minimized with US-guided access to reduce the chance of inadvertent arterial injury and by using the smallest possible vascular sheath. If pericatheter bleeding occurs, the thrombolytic infusion rate should be reduced or the infusion should be stopped until hemostasis is achieved by means of compression or upsizing of the sheath.

The benefits of using pharmacomechanical CDT rather than conventional CDT include reduced lytic agent dose, reduced procedural time, shortened stay in the intensive care unit, and fewer venography examinations. Overnight hospital admission—or even same-day discharge—has become feasible, as reported in the PEARL (Peripheral Use of AngioJet Rheolytic Thrombectomy with a Variety of Catheter Lengths) registry study, in which 73% of patients were treated in less than 24 hours, and 36% of patients, in less than 6 hours (32). The effectiveness of the Trellis system in single-session treatments also has been demonstrated, with a reported mean treatment time of 91 minutes per limb (29). As a result, the use of pharmacomechanical CDT has superseded the use of standard CDT in many modern practices. However, it is important to note that the thrombus reduction and symptom improvement achieved with pharmacomechanical CDT have not been shown to be substantially better (33).

Indications for Use of Standard CDT and Pharmacomechanical CDT

Consensus guidelines for the use of CDT and pharmacomechanical CDT for acute DVT have been developed by several major medical societies and reflect the controversy regarding the use of these treatment approaches. The Society of Interventional Radiology, Society for Vascular Surgery, and American Heart Association have established concordant guidelines that support the use of CDT and pharmacomechanical CDT for acute iliofemoral DVT in recently ambulatory patients with good functional status (5,14,34). However, the American College of

Chest Physicians recommends the use of anticoagulation alone, without adjunctive CDT, for acute proximal DVT (35).

Interventional therapy for infrainguinal DVTs is even more controversial because compared with iliac DVTs, these thromboses are more likely to recanalize and are associated with a lower incidence and severity of associated PTS (36) and a lower risk of recurrent venous thromboembolism (37). Approximately 50% of the CaVenT study population included patients with DVT extending to only the proximal femoral veins, and the treatment in these patients led to a substantial decrease in PTS cases; this finding suggests the potential for therapeutic benefit in this group. However, it remains unclear whether the added benefit of endovascular therapy, as compared with anticoagulation, merits the added risks of procedural complications. Currently, CDT is not generally recommended for the treatment of patients with isolated femoropopliteal involvement; anticoagulation is the most appropriate therapy for this group. However, CDT can be considered for acute DVT involving the upper half of the femoral vein in extremely symptomatic younger patients with refractory disease who have undergone anticoagulation therapy for 5 days (38).

Stent Placement

Residual venous stenoses that develop after standard or pharmacomechanical CDT for proximal DVT are common, but the indications for adjunctive venous stent placement performed in conjunction with either CDT procedure are poorly defined (39), and the rates of stent placement vary widely between studies. Current guidelines suggest that short-segment stenoses in iliocaval vessels are appropriate targets for stent placement (34,40), whereas femoropopliteal stenoses should be addressed with angioplasty alone. Stent placement is not necessary for small volumes of non–flow-limiting residual thrombus, particularly in patients who can undergo anticoagulation therapy. Stent placement has been reported to facilitate improved rates of venous patency, as evidenced by registry data that indicated higher 12-month venous patency rates for limbs with stents (74%) versus limbs without stents (53%) ($P < .001$) in patients with iliofemoral DVT who were treated with CDT (25). Conversely, not placing a stent to address residual proximal venous stenosis may predispose the patient to reduced venous patency and a higher rate of chronic symptoms. The relatively modest decrease in PTS rate seen after CDT in the CaVenT study, as compared with that seen in the other CDT studies, may have been due in part to the relatively low rate of adjunctive venous stent placement (17%). The durability of patency after stent placement for postthrombotic stenoses has been reported to be excellent, with up to 83% primary patency and 93% patency at 10 years (41). Reported rates of venous patency after stent placement for acute iliofemoral DVT in May-Thurner syndrome also have been favorable: up to 92% patency at 2 years (42). Technical issues associated with stent placement to consider include the identification of normal venous segments to serve as the proximal and distal landing zones and the importance of avoiding the placement of stents across the inguinal ligament, if possible, to prevent the increased risk of early in-stent restenosis. The only absolute contraindications to stent placement are noncorrectable coagulopathy and infection.

Conclusion

Compared with anticoagulation alone, endovascular DVT removal techniques—including CDT, pharmacomechanical CDT, and percutaneous mechanical thrombectomy—enable more rapid recanalization of affected veins and thereby reduce the severity of venous valvular damage. The use of these endovascular approaches also potentially decreases the frequency of long-term complications such as PTS. Current evidence supports the use of CDT for acute iliofemoral DVT; however, its use for infrainguinal DVT, which is less symptomatic and involves a lower risk of PTS, remains controversial. Owing to the continued evolution of endovascular technologies and prospective examinations to determine how they can be applied optimally, this group of techniques shows promise as adjunctive conventional therapies for proximal DVT.

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