Reporting Standards for Endovascular Treatment of Lower Extremity Deep Vein Thrombosis

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Abbreviations: DVT = deep venous thrombosis, INR = international normalized ratio, IVC = inferior vena cava, PE = pulmonary embolism, PTS = post-thrombotic syndrome, PTT = partial thromboplastin time, QOL = quality of life, SVS = Society for Vascular Surgery, VCSS = Venous Clinical Severity Score, VSDS = Venous Segment Disease Score, VTE = venous thromboembolism

THE feasibility of using endovascular techniques to treat lower extremity deep vein thrombosis (DVT) has been documented in numerous articles within the peer-reviewed radiology literature (1,2). Randomized trials are in progress to evaluate the efficacy of these therapies, but physicians are currently compelled to base endovascular DVT treatment decisions on published studies of less robust scientific design. Unfortunately, extreme variation in the descriptions of DVT patient populations, endovascular treatment methods, and outcomes assessment confounds accurate comparison of the existing studies and diminishes their relevance to the greater community of physicians who treat DVT. The purpose of this document is to improve the quality and relevance of DVT research published in the radiology literature by recommending basic guidelines for reporting the results of clinical DVT research studies.

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CURRENT STATUS OF RESEARCH REPORTING

The current document was produced in a cooperative effort between three Society of Interventional Radiology (SIR) committees: the DVT Research Committee of the SIR Venous Forum, the DVT Standards Committee of the SIR Venous Forum, and the SIR Technology Assessment Committee. To maintain consistency with previous efforts of nonradiology subspecialty organizations to standardize DVT reporting, many terms and definitions that are widely accepted by the scientific community have been incorporated into this document. Adoption of this common lexicon is expected to enhance the ability of interventional radiologists to effectively communicate the results of endovascular DVT therapies in terms that are meaningful to the many nonradiologists who treat and study DVT.

In 1988, a joint subcommittee of the Society for Vascular Surgery (SVS) and the International Society for Cardiovascular Surgery first published standards for reporting the results of surgical procedures to treat venous disease (3). In 1994, the American Venous Forum introduced the "CEAP" system, which was designed to enable classification of cerebrovascular disease based on its clinical manifestations (C), etiologic factors (E), anatomical distribution of disease (A), and underlying pathophysiologic findings (P). In 1995, the SVS's original reporting standards were revised to incorporate the CEAP system, a "Clinical Score," and a "Disability Score" (4). In 2000, the American Venous Forum's subcommittee on venous outcomes assessment observed that the CEAP classification was a useful descriptive tool but that it had too many static elements to be effective in monitoring

Table 1
Revised CEAP Classification of Chronic Venous Disease

C	Clinical signs (grade 0-6), supplemented by A for asymptomatic and S for symptomatic presentation
E	Etiologic classification (Congenital, Primary, Secondary)
A	Anatomic distribution (Superficial, Deep, or Perforator, alone or in combination)
P	Pathophysiologic dysfunction (Reflux or Obstruction, alone or in combination)

"C" (Clinical) classification	
Class 0	No visible or palpable signs of venous disease
Class 1	Telangiectases or reticular veins
Class 2	Varicose veins
Class 3	Edema
Class 4a	Skin changes including pigmentation or venous eczema
Class 4b	Skin changes including lipodermatosclerosis
Class 5	Healed venous ulceration
Class 6	Active venous ulceration

"E" (Etiologic) classification	
Ec (Congenital)	The etiology of the chronic venous disease has been present since birth
E_P (Primary)	Idiopathic chronic venous disease
Es (Secondary)	Chronic venous disease with known etiology (e.g., post-thrombotic)
En	No venous cause identified

"A" (Anatomic) classification	"P" (Pathophysiologic) classification
Superficial veins (A_S)	Reflux (P_R)
Deep veins (A_D)	Obstruction (P_O)
Perforating veins (A_P)	Both (P_{RO})
No venous location identified (An)	No venous pathophysiology seen (Pn)

Example: A patient with healed ulcerations known to be related to post-thrombotic syndrome, with documented reflux and obstruction would be classified as $C_5E_SA_DP_{RO}$.

change in disease status with treatment (5). To move beyond disease description to systematic outcomes assessment, the subcommittee recommended adoption of three separate scoring systems with which to categorize the clinical severity (Venous Clinical Severity Score, a substantially improved version of the original "Clinical Score"), anatomical/pathologic severity (Venous Segmental Disease Score, which combines the anatomical and pathologic elements of the CEAP), and disability (Venous Disability Score) of chronic venous disease. In 2004, the CEAP classification system was further refined; the revised version is presented in **Table 1** (6).

Many elements of the population description and outcomes assessment recommendations of the surgical societies have been incorporated into this document and should be easily adopted by interventional radiologists treating DVT. However, two major modifications have been made to increase their relevance to endovascular DVT therapies. First, standardized terminology for describing endovascular DVT treatment methods is recommended based on the consensus opinion of expert interventional radiologists. Second, discussion of the key DVT outcomes of interest has been modified to recognize the recent development and partial validation of several questionnaire measures to assess post-thrombotic syndrome and quality of life. In arriving at the current recommendations, every effort was made to remain consistent with the existing SIR documents addressing General Principles for Evaluation of New Interventional Technologies and Devices and Reporting Standards for the Treatment of Acute Limb Ischemia with Use of Transluminal Removal of Arterial Thrombus (7,8). In this fashion, the committee members have striven to create a useful template for clinical DVT research reporting that is relevant to current interventional practice.

POPULATION DESCRIPTION

An accurate population description serves several important purposes: (a) it enables a reader to determine whether a study is relevant to his or her patient population; (b) it helps to delineate which patient subsets are likely to benefit from the intervention being described; and (c) it facilitates meaningful comparison with other studies describing patient cohorts who were treated with the same or different medical, surgical, or interventional therapies. Detailed population description is particularly essential for DVT patient cohorts, since they can exhibit enormous variation in their defining characteristics (9). First and foremost, standardized definitions

should be used to describe the nature, anatomical extent, and clinical severity of venous disease processes. The following definitions are widely accepted by the general medical community:

Venous thromboembolism (VTE) refers to the single common disease entity with two principal manifestations: DVT and pulmonary embolism (PE) (10). A patient with a proved episode of DVT and/or PE is said to have had an episode of VTE. In describing the baseline incidence of DVT and PE in a patient population, it is important to recognize that therapies directed at one VTE manifestation often affect the incidence, progression, and response to therapy of the other manifestation. For example, a population of iliofemoral DVT patients is expected to have a high baseline incidence of PE (11). In a thrombolysis study, the number of patients with preexisting PE would be important to describe initially to avoid attributing any PE observed later in the treatment process to the treatment itself.

Pulmonary embolism (PE) refers most commonly to the intravascular migration of a venous thrombus to the pulmonary arterial circulation.

Proved PE refers to PE proved by a positive pulmonary angiogram, an unequivocally positive helical CT scan, a high probability ventilation-perfusion scan, or autopsy. PE is described as *symptomatic PE* (patient had clinical PE symptoms and/or signs such as chest pain, dyspnea, hemoptysis, palpitations, or tachycardia) or *asymptomatic PE* (PE was detected on an imaging study in a patient without suggestive symptoms).

Suspected PE refers to PE suspected based on clinical symptoms and/or signs but for which definitive diagnosis has not been made by imaging or autopsy.

Deep vein thrombosis (DVT) refers to the presence of thrombus within a deep vein of the body as proved by diagnostic imaging. For the lower extremity, this may include the calf veins (anterior and posterior tibial veins, peroneal veins, deep muscular veins), popliteal vein, femoral vein (formerly known as the superficial femoral vein), deep femoral vein, common femoral vein, iliac vein, and/or inferior vena cava (12).

Post-thrombotic syndrome (PTS) refers to a symptom complex that is commonly observed after one or more episodes of DVT. PTS is often characterized by limb edema, heaviness, pain, venous claudication, and limb hyperpigmentation, with a minority of patients developing severe manifestations such as venous ulceration.

Risk Factors and Predisposing Conditions

The conditions listed below represent independent risk factors for DVT and may influence its frequency of occurrence, clinical course, response to treatment, and likelihood of recurrence. In general, the presence of irreversible risk factors or idiopathic DVT confers a higher risk of recurrent DVT than reversible or time-limited risk factors.

1. Prior history of DVT. A prior episode of proved lower extremity DVT is a strong independent risk factor for a subsequent episode (13). Patients with residual venous thrombus on follow-up duplex US examination are at particularly high risk for recurrent VTE episodes (14). Knowledge of a history of prior DVT may influence the duration of anticoagulant therapy, indicate placement of an inferior vena cava (IVC) filter, or temper expectations for the results of endovascular therapy. For example, a population of acute iliofemoral DVT patients with a high incidence of prior DVT is expected to differ significantly from a population of patients without prior DVT with respect to the incidence and severity of PTS after catheter-directed thrombolysis.

2. Postoperative state and/or trauma. Major surgical procedures and bony fractures immobilize the patient and tilt the thrombolytic/hemostatic balance toward thrombosis. Patients particularly prone to DVT include those with pelvic and limb fractures and those undergoing neurosurgical, orthopedic, spinal, and major abdominal operations (15). DVT patient populations with a high incidence of recent surgery and/or trauma may be expected to have a higher incidence of bleeding complications with antithrombotic or fibrinolytic therapy.

3. Immobilization. Immobilization from illness or injury is a risk factor for DVT (16). The cause and duration of immobilization also influence the risk of DVT, with paraplegic patients being at particular risk (17).

4. Malignancy. The presence of malignancy is a major independent risk factor for DVT and recurrent VTE (18). Patients with widespread metastases and those with mucinous adenocarcinomas and other specific histologies are thought to be at particularly high risk. The presence of malignancy can significantly alter the type of anticoagulant therapy recommended, since low molecular weight heparins are associated with lower rates of recurrent VTE than vitamin K antagonists in cancer patients (19,20). In addition, lower 2-year primary patency rates have been observed in cancer patients treated with endovascular therapy compared with patients with benign causes of DVT (21). Prevention of PTS may be less of a priority for cancer patients with short life expectancy, and this can mitigate against the use of aggressive endovascular DVT therapies.

5. Inherited or acquired coagulation abnormality. Hematologic abnormalities that predispose patients to primary or recurrent VTE include factor V Leiden mutation, prothrombin gene mutation, antithrombin III deficiency, protein C and protein S deficiencies, lupus anticoagulant, antiphospholipid antibody syndrome, hyperhomocystinemia, and plasma hyperviscosity states (22–26).

6. Pregnancy and postpartum state. Pregnant and postpartum women are at risk for DVT (27,28). Pregnancy is a relative contraindication to thrombolysis.

7. Hormonal therapy. The use of hormonal therapy for contraception or other medical purposes is a risk factor for DVT (29). The type and duration of hormonal therapy also probably play a role in the development of thrombosis.

8. IVC filters. In patients with proximal DVT who receive concomitant anticoagulation, IVC filters reduce the early risk of PE but increase the rate of recurrent DVT (30). The presence of a filter may also increase the technical difficulty associated with endovascular treatment of IVC thrombosis (31).

9. Other factors. Extreme obesity, varicose veins, and congestive heart

failure have been inconsistently identified as independent DVT risk factors (32).

A cumulative risk factor scoring system has been described but is not included in this document because its grading system does not accurately reflect the relative risk of DVT conferred by each individual risk factor and because it does not account for patients with idiopathic DVT (ie, no known risk factor) (3). Patients with idiopathic DVT have a higher risk of recurrent DVT than patients with time-limited risk factors.

Major Comorbidities

The presence of major comorbidities in a patient cohort may reduce the clinical success rate and increase the rate of complications with treatment. Conversely, exclusion of patient subsets due to comorbidity can bias DVT populations, and this should be borne in mind when comparing patient cohorts. For example, exclusion of PE patients from a DVT study might indicate better clinical status of the included patient population.

1. Bleeding risks. Bleeding complications in DVT patients may be caused by anticoagulant therapy, thrombolytic therapy, or endovascular procedure-related vascular trauma (33). Knowledge of the incidence of additional risk factors for bleeding in the population can therefore improve meaningful comparison of bleeding complication rates between studies. Such risk factors include active bleeding; previous or current intracranial disease; recent trauma, surgery, or percutaneous procedures; severe hepatic dysfunction; gastrointestinal bleeding history; and severe uncontrolled hypertension.

2. Pulmonary or cardiac disease. Preexisting pulmonary or cardiac disease can increase the clinical severity of any complications that are encountered and is an important indicator of the overall health of the patient population. The presence and severity of pulmonary hypertension and/or right heart dysfunction is particularly important. On the one hand, catheter manipulations may fragment thrombus and cause procedure-related PE. On the other hand, any pulmonary emboli may be dissolved by circulating thrombolytic agents.

3. Renal failure. Preexisting renal dysfunction can increase the rate of contrast-related renal failure after endovascular intervention and is an important indicator of the overall health of the patient population.

4. Active infection. Active bloodstream infection is a relative contraindication to some endovascular procedures. Because DVT patients commonly present with fever or leukocytosis, or both, the diagnosis of bloodstream infection should be based on positive blood cultures or septic hemodynamics.

5. Overall performance status. The use of standardized instruments to describe overall patient performance status (for example, ASA classification) may improve comparison of the relative overall health of different populations (34).

Details of Prior or Concomitant Treatment

Accepted DVT treatments that can meaningfully affect evaluation of therapeutic interventions include bed rest with leg elevation, early ambulation protocols, compression stockings, anticoagulant therapy, antiplatelet therapy, surgical thrombectomy or bypass, endovascular thrombus removal methods, balloon angioplasty, stent placement, and IVC filter placement (19,35–37).

Baseline Clinical Presentation of Venous Disease

The pretreatment clinical status of venous disease in the population should be characterized in a manner that permits comparison between patient cohorts:

1. *Acute DVT* refers to venous thrombosis for which symptoms have been present for 14 days or less or for which imaging studies indicate that venous thrombosis occurred within the last 14 days (33). The primary symptoms of acute DVT are limb swelling and pain. Standardized measurement of limb circumferences at the same craniocaudal level can be used to quantify the degree of limb swelling. Pain can be graded using a number of validated pain scales (for example, the Visual Analog Scale) (38). *Phlegmasia* refers to a characteristic clinical picture in which DVT causes massive swelling of the entire extremity. *Phlegmasia alba dolens* is not associated with cyanosis. In contrast, *phlegmasia cerulea dolens* is associated with cyanosis and can lead to arterial insufficiency, compartmental compression syndrome (compartment syndrome), venous gangrene, and limb amputation (39).

2. *Subacute DVT* refers to venous thrombosis for which symptoms have been present for 15 to 28 days or for which imaging studies indicate that venous thrombosis occurred within this time interval. This designation, while not in common practice, is included because the expert committee members believed that a difference in endovascular treatment response rates exists between patients treated in this time window compared with patients treated earlier or later (33).

3. *Chronic DVT* refers to venous thrombosis for which symptoms have been present for more than 28 days or for which imaging findings document the presence of venous thrombosis more than 28 days before (33). Chronic venous disease may manifest with a broad range of symptoms that can vary in severity throughout the day. There are several methods by which the baseline clinical severity of chronic venous disease in a population can be described by physician assessment. First, the "C" (clinical) component of the CEAP system stratifies patients into six venous disease categories of increasing severity (**Table 1**) (6). Second, the Venous Clinical Severity Score (VCSS) is an excellent scoring system with which to follow the progress of chronic venous disease in individual patients and to compare patient cohorts (**Table 2**) (5). Although not completely validated for all DVT patient populations, the VCSS correlates well with CEAP class and with US findings of venous disease (40–42). Third, the Venous Disability Score is an easily applied scoring scheme in which venous disease severity is grossly categorized according to the degree to which it limits a patient's normal activities (**Table 3**) (40). Patient symptom self-assessment can also be extremely useful in describing disease severity and quality-of-life (QOL) in DVT populations. Symptom- or disease-specific QOL questionnaires that have been at least partially validated in venous disease populations include

Table 2
Venous Clinical Severity Score

Attribute	Absent = 0	Mild = 1	Moderate = 2	Severe = 3
Pain	None	Occasional, not restricting activity or requiring analgesics	Daily, moderate activity limitation, occasional analgesics	Daily, severely limits activities, regular use of analgesics
Varicose veins*	None	Few, scattered: branch VVs with competent GSV/LSV	Multiple: single segment GSV/LSV reflux	Extensive: multisegment GSV/LSV reflux
Venous edema†	None	Evening ankle edema only	Afternoon edema above ankle	Morning edema above ankle requiring activity change, elevation
Skin pigmentation	None, or focal, low intensity (tan)	Diffuse, but limited in area and old (brown)	Diffuse over gaiter distribution (lower third) or recent pigmentation (purple)	Wider distribution (above lower third) and recent pigmentation
Inflammation	None	Mild cellulitis, limited or marginal area around ulcer	Moderate cellulitis, involves most of gaiter area	Severe cellulitis (lower third or above) or venous eczema
Induration	None	Focal, circum-areolar (<5 cm)	Medial or lateral, less than lower third	Entire lower third or more
Total number of ulcers‡	0	1	2–4	>4
Active ulceration, duration	None	<3 months	>3 months, <1 year	Not healed >1 year
Active ulcer, size	None	<2 cm diameter	2–4 cm diameter	>4 cm diameter
Compressive therapy§	Not used or not compliant	Intermittent use of stockings	Wears elastic stockings most days	Full compliance stockings + elevation

Qualifying comments:
* To ensure differentiation between the C1 and C2 CEAP classes, "varicose" veins must be >4 mm diameter to qualify for inclusion here. Occasional or mild edema and focal pigmentation over varicose veins does not qualify for inclusion under the two subsequent attributes.
† Presumes venous origin by characteristic, eg brawny (not pitting or spongy) edema, with significant effect of standing/limb elevation and/or other clinical evidence of venous etiology, ie varicose veins, history of DVT. Edema must be regular finding, eg daily occurrence.
‡ Total number equals active and healed.
§ Sliding scale to adjust for background differences in use of compressive therapy.

Table 3
Venous Disability Score

0 = Asymptomatic
1 = Symptomatic but able to carry out usual activities* without compressive therapy
2 = Can carry out usual activities* only with compression and/or limb elevation
3 = Unable to carry out usual activities* even with compression and/or limb elevation

* Usual activities = patient's activities before onset of disability from venous disease.

the CIVIQ, Villalta, Mathias, and VEINES-QOL/Sym questionnaires (**Table 4** and Appendix 1) (43–49). General QOL measures have included the SF-36 and Nottingham Health Assessment (50,51).

Venous gangrene is full-thickness skin necrosis caused by DVT. Blistering indicates partial thickness necrosis and is considered early venous gangrene (4).

4. Acute-on-chronic DVT refers to venous thrombosis that has both chronic (>28 d) and acute (≤14 d) components, as indicated by symptom history or imaging findings (33).

Pretreatment Anatomical/ Physiologic Assessment

The following categorization scheme should be consistently applied to describe the anatomical extent of DVT:

Proximal DVT refers to complete or partial thrombosis of the popliteal vein, femoral vein, deep femoral vein, common femoral vein, iliac vein, and/or IVC. Proximal DVT is often complicated by PE (19). Proximal DVT can be further subclassified as follows:

Femoropopliteal DVT refers to complete or partial thrombosis of the popliteal vein, femoral vein, and/or deep femoral vein.

Iliofemoral DVT refers to complete or partial thrombosis of any part of the iliac vein and/or the common femoral vein, with or without associated femoropopliteal DVT (33,52). Published studies differ in terms of whether patients with common femoral vein thrombosis and a patent iliac vein are considered to have iliofemoral DVT. After consideration, the consensus opinion of the committee members is that by obstructing outflow from both the femoral and deep femoral veins,

Table 4
Selected Venous Disease Questionnaire Measures

Measure	Type	Study	Intended Population
Villalta Scale	Post-thrombotic symptoms	Villalta 1994 (43) Prandoni 1996 (18) Brandjes 1997 (35)	DVT
CIVIQ	Disease-specific HRQOL	Launois 1996 (45) Ziegler 2001 (44)	CVD due to DVT or VR
VEINES-QOL/Sym	Disease-specific HRQOL	Lamping 1998 (47) Kahn 2002 (87) Lamping 2003 (48) Kahn 2004 (49)	CVD due to DVT or VR
Mathias Scale	Disease-Specific HRQOL	Mathias 1999 (46) Comerota 2000 (91)	DVT

CVD = chronic venous disease; DVT = deep vein thrombosis; HRQOL = health-related quality-of-life; VR = primary venous reflux.

common femoral vein thrombosis produces a clinical picture that is essentially identical to iliac vein thrombosis. Therefore, the committee members do recommend that such patients be categorized as having iliofemoral DVT. Iliofemoral DVT carries a higher risk of recurrent VTE and possibly also a greater risk of PTS (52,53).

Calf vein DVT refers to complete or partial thrombosis of one or more deep calf veins, including the anterior tibial veins, posterior tibial veins, peroneal veins, and deep muscular veins. Isolated calf vein DVT rarely leads to PE (19). When calf vein DVT propagates into the popliteal vein, it is considered proximal DVT.

Diagnostic venography represents the criterion standard imaging modality with which to confirm the presence and define the anatomical extent of DVT (54). The hallmark venographic finding of DVT is the visualization of intraluminal filling defects. Other findings may include abrupt cut-off of a vein, lack of opacification, and/or intraluminal septations or webs. In nearly all instances, when information from another diagnostic modality is not consistent with venography, the venographic result should be relied upon.

Ideally, each patient being considered for endovascular therapy should undergo baseline venographic characterization of the entire venous system of the limb from calf through IVC. This provides the most accurate determination of the baseline extent of thrombosis, which is necessary for meaningful evaluation of several major DVT outcomes such as the incidences of progressive DVT and recurrent VTE. However, it is recognized that this may be difficult to achieve in actual clinical practice. Many experienced interventionalists do not routinely image or treat thrombus that extends below the popliteal vein, and the quality of calf venography can vary somewhat with operator experience. It is recognized that calf venography may not be clinically warranted in certain situations, for example, when iliocaval DVT is present but does not extend into the femoral vein. In clinical trials, patients may be randomized to a control arm in which endovascular therapy is not given, and it may not be deemed ethical to subject these patients to invasive venographic testing.

In these situations, compression duplex sonography can be relied on to evaluate the femoropopliteal and common femoral veins with extremely high accuracy (55–57). The hallmark finding of DVT on duplex sonography is venous noncompressibility. Other findings may include visualized intraluminal material, absence of flow on augmentation, lack of respiratory variation, and incomplete color filling.

The calf veins and iliocaval venous system pose a greater challenge to clinical DVT research efforts. Although clinical treatment decisions can be reliably based on noninvasive imaging in the overwhelming majority of DVT patients, the much greater detail needed to accurately assess anatomical outcomes in clinical research studies is often difficult to obtain. Duplex sonography has only 70% to 85% accuracy for calf vein thrombosis but is nevertheless the best available noninvasive modality with which to characterize its extent (54,58,59). Duplex sonography of the iliac vein may be limited by poor venous visualization owing to its deep position in the pelvis, although it can be diagnostic in many instances. A well-opacified contrast-enhanced CT scan or MR imaging scan is likely to be accurate in diagnosing iliac vein DVT when venography cannot be performed (60,61). However, it must be noted that CT and MR imaging have not undergone rigorous validation studies for DVT diagnosis. For these reasons, venographic definition of the complete anatomical extent of DVT should be sought whenever possible. When this is not possible, reliance on a combination of duplex ultrasound (calf veins) and CT scanning or MR imaging (iliocaval veins) is recommended.

Partial physiologic evaluation of the venous system can be performed in several ways: a) Endovascular catheter access permits the acquisition of direct venous pressure measurements to characterize venographically identified abnormalities. The limited available evidence suggests that a resting mean pressure gradient of 2 mm Hg or less is normal and that a gradient of 5 mm Hg or greater indicates hemodynamically significant stenosis (62–64); b) Duplex sonography can diagnose venous reflux and estimate flow veloc-

Table 5
Venous Segmental Disease Score*

Reflux	Obstruction (or excised/ligated)
1/2 Lesser saphenous	
1 Greater saphenous	1 Greater saphenous (only if from groin to below knee)
1/2 Perforators, thigh	
1 Perforators, calf	
2 Calf veins, multiple (PT alone = 1)	1 Calf veins, multiple
2 Popliteal vein	2 Popliteal vein
1 Superficial femoral vein	1 Superficial femoral vein
1 Profunda femoris vein	1 Profunda femoris vein
1 Common femoral vein & above†	2 Common femoral vein
	1 Iliac vein
	1 IVC
10 = Maximum reflux score‡	10 = Maximum obstruction score‡

* Based on presence of venous segmental reflux or obstruction as assessed by appropriate venous imaging, duplex US or venogram.
† Normally there are no valves above the common femoral vein.
‡ Not all of the 11 segments listed can be involved in reflux or obstruction.
Qualifying comments: *Reflux* means that all the valves in that segment are incompetent. *Obstruction* means there is total occlusion at some point in the segment or greater than 50% narrowing of at least half of the segment. Most segments are assigned 1 point, but some segments have been weighted more or less to fit with their perceived significance, eg increasing points for common femoral or popliteal obstruction and for popliteal and multiple calf vein reflux and decreasing points for lesser saphenous or thigh perforator reflux. Points can be assigned for both obstruction and reflux in the same segment. This will be uncommon but can occur in some post-thrombotic states, potentially giving secondary venous insufficiency higher severity scores than primary disease.

ities; and c) plethysmography can determine the postexercise venous refill time and thereby estimate the volume of venous reflux, with some limitations (65).

The Venous Segmental Disease Score (VSDS) incorporates the "A" (anatomical) and "P" (physiologic) parts of the CEAP system into a 10-point reflux scale and a 10-point obstruction scale (**Table 5**) (43). The VSDS correlates well with the CEAP system and can be used to score the combined results of imaging and physiologic testing (45).

Recommendations for Reporting

Basic demographic description must be provided, including age, gender, and affected limb (right, left, or both) for all patients in each treatment group. For studies including patients with IVC involvement, both the number of patients and the number of symptomatic limbs must be stated. For categorical variables (ie, gender), the proportions of subjects in each category must be reported. For continuous variables (ie, age), the mean or median (nonparametric variables), SD or SEM, and range must be reported. The study inclusion and exclusion criteria must be explicitly stated, and the method of assigning treatments to subjects must be described. When possible, patient selection should be stratified by anatomical DVT extent, symptom duration, and clinical severity.

The proportion of patients presenting with DVT, PE, both DVT and PE, or neither must be stated for the entire population and for each treatment group. Authors must indicate how the presence of DVT or PE was established. Description of how many episodes of proved PE were symptomatic versus asymptomatic is highly recommended.

The proportion of patients with each of the following risk factors should be stated for the patient population and for each treatment group: prior DVT history, recent (< 1 mo) major surgery or percutaneous procedures, recent (< 1 mo) trauma or immobilization, presence of malignancy, known inherited or acquired coagulation abnormality, pregnancy or postpartum state, hormonal therapy, or the presence of an IVC filter. Inclusion of information pertaining to the type and timing of recent surgery, type and extent of malignancy, type of coagulation disorder, type of hormonal therapy, and presence of paraplegia in the patient population is highly recommended. The proportion of patients with additional risk factors for major bleeding (especially intracranial disease, liver disease, and gastrointestinal bleeding history), cardiopulmonary disease (particularly pulmonary hypertension), renal dysfunction, or infective conditions must be specified. Inclusion of information pertaining to the severity of these conditions is highly recommended. The thresholds for study inclusion with regard to acceptable hematocrit, platelet count, international normalized ratio (INR), and partial thromboplastin time (PTT) must be stated. If therapeutic interventions (ie, vitamin K administration, transfusion) were allowed to bring these parameters within the acceptable range, this should be stated.

The proportion of patients who received ongoing or previous DVT or PE treatment using any of the following methods must be stated: bed rest with leg elevation; early ambulation protocol; compression stockings (specifying the stocking type, length, amount of compression, and compliance level is highly recommended); anticoagulant

therapy (specifying the agent, duration of therapy, and target INR or PTT if applicable is required); surgical or endovascular procedures (specifying the procedure type and extent is required); and/or IVC filter placement (specifying the type is required, providing the duration of implantation and timing of removal are recommended).

The baseline clinical presentation of venous disease in the population must be described. The proportion of patients with acute, subacute, and chronic DVT in the patient population and in each treatment group must be specified. For patients with acute DVT, the number of patients with limb swelling and/or pain must be specified. The use of standardized leg circumference measurements and validated pain scales are highly recommended in describing acute symptom severity. The number of patients with phlegmasia cerulea dolens, compartmental compression syndrome, or signs of arterial insufficiency must be indicated. For studies evaluating treatment of chronic venous disease, the mean or median CEAP clinical class, VCSS, Venous Disability Score, or venous disease-specific patient self-assessment questionnaire score of the population must be provided; reporting of more than one of these parameters is highly recommended. The use of a general health-related QOL patient self-assessment instrument is also recommended.

The baseline anatomical extent of thrombosis and the imaging methods of diagnosis must be specified. The proportion of patients with calf vein DVT, femoropopliteal DVT, iliofemoral DVT, infrarenal IVC involvement, and suprarenal IVC involvement must be reported. Baseline bilateral duplex US evaluation for the presence of venous reflux is also highly recommended for all patients.

TREATMENT DESCRIPTION

Venous Access

Endovascular DVT interventions require catheter access in at least one part of the venous system. Access may be obtained in open surgical fashion (using a surgical cutdown and/or venotomy) or in percutaneous fashion. When percutaneous deep venous access is obtained, US guidance is commonly used. Fluoroscopy can also be used either in conjunction with US or as the sole imaging modality.

Venous access can be antegrade (in the direction of normal venous flow) or retrograde (against the direction of normal venous flow). For the treatment of lower extremity DVT, antegrade access is commonly obtained in the popliteal vein, posterior tibial vein, soleal vein, anterior tibial vein, and/or peroneal vein (1,66). When using antegrade access, a site is ideally chosen below the caudal extent of the thrombus. Retrograde access is commonly obtained from the internal jugular vein, although other major deep veins can also be used. Common femoral vein access can be antegrade or retrograde and can be obtained in the affected ipsilateral limb or in the contralateral limb. For example, the use of right common femoral vein access to treat a left iliofemoral DVT would be classified as retrograde contralateral.

Transluminal Thrombus Removal Methods

The following sections describe the most common methods of performing transluminal removal of thrombus from the deep venous system:

Pharmacologic thrombolysis refers to administration of drugs with thrombolytic activity. When reporting the results of pharmacologic thrombolysis, the *thrombolytic infusion time* is the total time during which the drug was infused. *Treatment time* is the total time from the start of the first thrombolysis procedure or the initial drug administration (whichever was first) to termination of the final follow-up procedure or of the infusion (whichever was last). Pharmacologic thrombolysis is subdivided according to the thrombolytic agent delivery method:

Systemic thrombolysis refers to pharmacologic thrombolytic agent delivery through an intravenous line, which is located distant from the affected extremity (8,67). The drug can be administered as a bolus (single dose) or as a continuous infusion.

Flow-directed thrombolysis refers to pharmacologic thrombolytic agent delivery through a pedal intravenous line placed within the affected extremity, with or without the use of tourniquets to intermittently compress the saphenous system to direct the drug into the deep venous system. The drug can be administered as a bolus or as a continuous infusion (68). Use of the term *locoregional thrombolysis* is discouraged, since this may be confused with intrathrombus thrombolysis.

Catheter-directed intrathrombus thrombolysis (CDT) refers to pharmacologic thrombolytic agent delivery through an infusion catheter or wire that is embedded within the thrombosed vein being treated (1,69). Multi-side-hole catheters are most commonly used for this purpose. The drug can be administered as a single or periodic bolus or as a continuous infusion (70). A *lacing dose*, in which a catheter is used to disperse a bolus dose of the thrombolytic drug throughout the thrombus, can also be given (71).

Mechanical thrombectomy refers to use of catheter-based mechanical devices that contribute to thrombus removal via fine (microscopic) thrombus fragmentation, maceration, or aspiration. When performed percutaneously, the term *percutaneous mechanical thrombectomy (PMT)* is used (2).

Pharmacomechanical thrombolysis refers to thrombus dissolution via any simultaneous use of pharmacologic thrombolysis and mechanical thrombectomy. Several specific methods may fall under this definition: a) *Pulse-spray pharmacomechanical thrombolysis* refers to a specific technique in which a thrombolytic drug is periodically forcefully injected into the thrombus using a multi-side-hole catheter (72). This technique is clearly distinguished from lacing, in which an intrathrombus bolus dose is given without any intended mechanical effect. b) Because fine thrombus maceration may enhance pharmacologic clot dissolution and vice versa, the use of any mechanical thrombectomy method while a pharmacologic thrombolytic drug is circulating constitutes a form of pharmacomechanical thrombolysis (73).

Adjunctive Mechanical Thrombus Removal Techniques

The following techniques are mechanical in nature but are not classified as mechanical thrombectomy methods because they do not produce fine (microscopic) maceration of thrombus.

Aspiration thrombectomy refers to the use of a syringe to aspirate thrombus from the clotted vein via a catheter or sheath (74).

Balloon thrombectomy refers to the use of catheter-mounted balloons (for example, a Fogarty balloon) to mobilize or extract thrombus.

Balloon maceration refers to the use of an angioplasty balloon to produce gross thrombus fragmentation or maceration. This is commonly done to enhance the rate of clot dissolution during pharmacologic thrombolysis.

Concomitant Medical Therapy

Supplemental antithrombotic therapy can be given during thrombolysis to augment the thrombolytic effect or to prevent new thrombus formation, or both. Parenteral agents that have been used include unfractionated heparin and glycoprotein IIb/IIIa inhibitors (75). *Therapeutic-level heparin* administration refers to the intravascular use of unfractionated heparin to raise the PTT to 1.5 to 2.5 times the control level. *Subtherapeutic heparin* refers to the intravascular use of unfractionated heparin at lower doses to prevent pericatheter thrombosis (PTT $<$1.5 times control).

Balloon Angioplasty, Stent Placement, and Inferior Vena Cava Filter Placement

When thrombus removal is completed or nearly completed, repeat venography is typically performed to evaluate for any venous stenoses that might have contributed to the initial thrombotic episode. At this point, *balloon angioplasty* may be used to dilate a visualized venous stenosis. This term should be used only when an angioplasty balloon is used with the specific intent of enlarging the venous lumen (unlike balloon maceration in which the specific intent is to increase the surface area of residual thrombus). *Stent placement* refers to use of a metallic endoprosthesis to enlarge and maintain the venous lumen. The timing of stent placement with respect to clot removal merits description, since stents can be used either for treatment of stenosis or to exclude residual thrombus from the vein lumen and thereby shorten the thrombolytic infusion time (76). *IVC filter placement* can also be employed to prevent PE either before or after endovascular thrombus removal methods are employed. Retrievable or permanent filters can be used.

Adjunctive Surgical Therapies

Arteriovenous fistula creation can be performed to improve flow and thereby maintain early patency after endovascular or surgical venous recanalization (21). In most cases, the fistula is taken down after a defined period of time.

Surgical thrombectomy refers to the use of open surgical techniques, including venotomy, to remove thrombus from the deep veins of the body (77,78).

Venous bypass refers to the surgical placement of a native or prosthetic conduit to bypass a segment of venous occlusion.

Recommendations for Reporting

When describing transluminal thrombus removal methodology, authors must clearly state what treatment was originally intended and what treatment was actually administered. This will facilitate intention-to-treat analysis of the data. For example, if the originally intended protocol for using a mechanical thrombectomy device to treat a DVT cohort did not include subsequent pharmacologic thrombolysis, this should be clearly stated. In that situation, patients who receive subsequent pharmacologic thrombolysis for residual thrombus should be reported as having failed stand-alone mechanical thrombectomy. In contrast, if the original treatment protocol was written to include mechanical thrombectomy followed by pharmacologic thrombolysis, then treatment success or failure can be assigned based on the results of treatment with the entire protocol (ie, both modalities in sequence).

The clinical setting in which patients received treatment (ie, outpatient, standard inpatient hospital bed, intermediate-care unit, or intensive care unit) must be specified.

The specific vein or veins accessed for endovascular DVT treatment must be indicated. Authors must state whether access was obtained percutaneously or via open surgery and whether the access was directed antegrade or retrograde. If imaging guidance was used, the specific modality must be indicated. Inclusion of how frequently antegrade venous access sites were below the caudal extent of thrombus is required.

The primary method of thrombus removal must be specified (pharmacologic thrombolysis, mechanical thrombectomy, pharmacomechanical thrombolysis, aspiration thrombectomy, balloon thrombectomy, or balloon maceration), and the chronological order in which the methods were used must be reported.

For studies evaluating pharmacologic thrombolysis, the thrombolytic agent, manufacturer, bolus dose (if given), initial hourly infusion dosage and solution concentration, total dose administered, thrombolytic infusion time, hematologic monitoring protocol, and parameters used for adjusting the dose must be specified. For studies including patients with IVC thrombosis or bilateral DVT, doses and infusion times for that patient subset must be reported separately and should be calculated per patient and per treated (symptomatic) limb. The route of drug administration (systemic, flow-directed, or catheter-directed intrathrombus) must be specified. For patients undergoing catheter-directed intrathrombus thrombolysis, the type of catheter (multi-side-hole vs. end-hole) catheter used to administer the drug must be specified. If a lacing dose was given, this must be specified. If flow-directed thrombolysis was performed, description of the tourniquet system (type, manufacturer, and method of use) is highly recommended. If balloon maceration or other methods to grossly macerate thrombus were used, the protocol for use must be described as well.

For studies evaluating mechanical thrombectomy, the device name, manufacturer, and model must be stated. The exact method of device use must be specified, especially for devices that can be used in multiple modes. For example, when describing use of the Angiojet, authors must state whether it was used with the effluent lumen open or occluded. Inclusion of the total device activation time is highly recommended.

For studies evaluating pharmacomechanical thrombolysis, the timing

of drug administration and mechanical thrombectomy device usage must be clearly indicated. If pulse-spray pharmacomechanical thrombolysis was used, this must be clearly stated.

If aspiration thrombectomy, balloon thrombectomy, or balloon maceration was used, the catheter system utilized must be specified along with the protocol for use.

The specific protocol for use of balloon angioplasty, stent placement, or IVC filter placement should be standardized within the protocol and must be described with reference to the timing and results of the transluminal thrombus removal methods. If balloon angioplasty was used, the specific vessel dilated and balloon diameter must be specified. Inclusion of the inflation pressure and duration of inflation is recommended. If stenting was performed, the vessel treated, stent type, manufacturer, size, and diameter to which the stent was dilated must be provided. If IVC filters were placed, the type, indication, timing of placement with respect to endovascular DVT treatment, intended duration (temporary vs. permanent), and timing of removal must be indicated. The type and extent of any adjunctive surgical methods used must be described.

The use of any concomitant medical therapy that may affect the coagulation pathway or platelet function must be described. If heparin was given, the dose, route of administration (ie, peripheral intravenous line vs. angiographic sheath), intended level of anticoagulation (therapeutic-level vs. subtherapeutic), and target PTT must be provided. The protocol used to monitor the level of anticoagulation must be described. If a vitamin K antagonist was used, the target INR must be described. Brief description of the protocols for periprocedure management and long-term use of anticoagulant and antiplatelet agents is also required.

OUTCOMES ASSESSMENT

Meaningful assessment of a DVT treatment should quantify its impact on several major outcomes of interest. The overall severity of chronic venous disease and its effect on QOL have historically been difficult to quantify because its symptoms and signs can vary significantly. A natural temptation has been to rely on surrogate endpoints that are easier to assess (eg, venographic patency), but this practice can be very misleading when these endpoints have not been statistically proved to correlate with the clinically meaningful outcomes (eg, QOL) (79). The following sections describe the major outcomes of interest for DVT patients. Because some endovascular DVT therapies may trade early risk for late benefit, investigators should report outcomes in as many of the following categories as possible.

Assessment of Treatment Safety

Deep venous thrombosis therapies have varying complication profiles. For treatments involving any pharmacologic agent, major or minor allergic reactions may be observed. Any invasive therapy can produce an infectious complication, and those that require conscious sedation or general anesthesia carry risks of cardiorespiratory compromise. *Major bleeding*, defined as intracranial bleeding or bleeding severe enough to result in death, surgery, cessation of therapy, or blood transfusion, is an important safety outcome of all DVT therapies involving antithrombotic agents (8). *Minor bleeding* is defined as less severe bleeding manageable with local compression, sheath upsizing, or dose alterations of a pharmacologic thrombolytic agent, anticoagulant, or antiplatelet drug (8). *Renal failure*, defined as a 20% or greater increase in serum creatinine level, can complicate any procedure in which iodinated contrast is used (80). Angioplasty and stenting procedures may be complicated by venous rupture and/or stent malposition or migration; these events may have no consequence or may cause significant problems such as bleeding or contralateral DVT. *Symptomatic* or *asymptomatic PE* can be caused by the underlying VTE disease process or by thrombus manipulation. Methemoglobinuria is an expected effect of many mechanical thrombectomy devices and is not a complication except when associated with renal failure or hemolysis, which is significant enough to result in death, surgery, cessation of therapy, or blood transfusion.

Any adverse event occurring during the time period beginning with the initial diagnostic venogram to 24 hours after the termination of therapy (including removal of venous access) must be considered procedure-related. Adverse events that are detected later than 24 hours can also be procedure-related, such as renal failure. The use of 30-day mortality rates is encouraged to enable comparison with other treatment methods.

Assessment of Treatment Efficacy

Although outcomes such as PE and PE-related death can be evaluated with short follow-up intervals, the time course for meaningful evaluation of the progression of chronic venous disease is significantly longer. Therefore, clinical follow-up should be graded as *short-term* (<1 y), *mid-term* (1–3 y), or *long-term* (>3 y).

Pulmonary Embolism and Late Pulmonary Dysfunction

Anticoagulant therapy drastically reduces the incidences of PE and PE-related death (19). In surviving patients, late complications of PE may include pulmonary arterial hypertension, chronic pulmonary thromboembolic disease, cor pulmonale, and various pulmonary function abnormalities. These problems can lead to death or QOL impairment and are therefore extremely important to quantify using objective means. Pulmonary function parameters of interest include right heart and pulmonary arterial pressure estimation using direct manometry or echocardiography, pulmonary vascular resistance, diffusion capacity, and pulmonary capillary blood volume.

Early and Late Limb Status

Early Symptom Relief.—Endovascular treatment may speed resolution of symptoms in acute DVT patients. Standardized limb circumference measurements and validated pain scales are effective and inexpensive instruments with which to document changes in limb symptomatology. *Progression of DVT* is defined as imaging proved extension of an existing DVT into at least one previously uninvolved venous segment. *Limb salvage* and *amputation-*

Table 6
Venographic Scoring Systems*

A. Marder Scoring System (different segments have differing maximum point values)

VENOUS SEGMENTS	POINTS	CRITERIA FOR SCORING SEGMENTS
Iliac	6	
Common femoral	4	Count Full Points for complete occlusion
Femoral	10	Proportionally Lower for partial occlusions
Popliteal	4	No Points for patent vein
Anterior tibials (paired)	4 (2 each)	
Posterior tibials (paired)	6 (3 each)	
Peroneals (paired)	6 (3 each)	
Total Score Possible:	40	

B. SVS Scoring System (each segment is worth 3 points)

VENOUS SEGMENTS	POINTS	CRITERIA FOR SCORING SEGMENTS
Tibial-soleal veins	3	
Popliteal vein	3	0 = patent
Femoral vein	3	1 = subsegmental, nonocclusive thrombus
Common femoral vein	3	2 = subsegmental, occlusive thrombus
Iliac vein	3	3 = occlusive thrombus throughout segment
Inferior vena cava	3	
Greater saphenous/branches	3	
Lesser saphenous/branches	3	
Total Score Possible:	24	

C. Venous Registry Index (each segment is worth 2 points)

VENOUS SEGMENTS	POINTS	CRITERIA FOR SCORING SEGMENTS
Inferior vena cava	2	
Common iliac vein	2	0 = completely free of thrombus
External iliac vein	2	1 = partially occluded
Common femoral vein	2	2 = completely occluded
Proximal half of femoral vein	2	
Distal half of femoral vein	2	
Popliteal vein	2	
Total Score Possible:	14	

* For each scoring system, the total thrombus score for a limb is the sum of the individual scores assigned to each venous segment. The maximum point value for each segment differs somewhat among the three scales, as do the criteria for scoring each segment.

free survival represent two additional outcomes of interest in the subset of DVT patients with phlegmasia cerulea dolens.

Immediate Venous Patency.—Immediate post-treatment venography is commonly performed in DVT patients undergoing endovascular intervention. *Anatomical success* can be defined in one of two ways, and preferably both: a) successful restoration of antegrade in-line flow in the treated vein with elimination of any underlying obstructive lesion (81). This is generally assessed on the final procedural venogram (ie, after adjunctive endovascular therapies are completed). Unfortunately, the degree of residual venous diameter narrowing needed to produce flow limitation and symptoms have not been characterized in the venous system. b) For studies evaluating transluminal thrombus removal methods, estimation of the *degree of thrombolysis* can be also be performed. This should be assessed on the venogram obtained after thrombus removal but before stent placement because stents can exclude residual thrombus and confer a venographically normal appearance even when residual thrombus is present, confounding accurate assessment of the thrombus removal methods. Venographic scoring systems that have been used in prior DVT studies include the Marder scale, SVS scale, and the Venous Registry Index (4,12,82) (**Table 6**). These scales can be used to classify patients as showing minimal or no thrombolysis (grade I, $< 50\%$ thrombus removal), partial thrombolysis (grade II, 50–95% thrombus removal), or complete thrombolysis (grade III, 95–100% thrombus removal).

Late Venous Patency and Recurrent Venous Thromboembolism.—The presence of residual thrombus increases the relative risk of recurrent VTE and PTS in DVT patients (13). Therefore, documenting its presence is important in the long-term risk stratification of DVT patients. *Recurrent VTE* is defined as the presence of a new proved PE or recurrent DVT in a patient with at least one prior episode of VTE. *Recurrent DVT* is defined as imaging-proved DVT involving a new venous segment or a previously involved venous segment for which symptomatic and imaging improvement had been obtained in a patient with at least one prior episode of DVT. *Primary patency* is defined as the time from the intervention to the

first occurrence of either thrombosis of the treated segment or to an intervention to maintain patency (8). *Primary assisted patency* is defined as the time from the intervention to the first occurrence of thrombosis, irrespective of any interval therapy to restore or maintain flow within the treated segment. *Secondary patency* is defined as the time from the intervention to the permanent loss of flow in the treated segment, irrespective of any interval therapies. *Early rethrombosis* refers to loss of primary assisted patency within 30 days after the intervention. *Late rethrombosis* refers to loss of primary assisted patency more than 30 days after the intervention. When possible, evaluation of patency should be performed using venography. However, when this cannot be performed, a combination of duplex US and pelvic CT scanning or MR imaging can be used according to the common practice of the institution.

Valvular Reflux.—Venous reflux is thought to be a critical pathophysiologic factor in the development of PTS (32). Late valvular assessment can be important to determine whether valvular preservation represents the mechanism underlying improved late limb status after DVT treatment. It is important to keep in mind, however, that valvular dysfunction represents a surrogate outcome measure in patients treated for DVT, and that the more clinically meaningful outcome measures for late limb status are PTS and health-related QOL.

Venous reflux is defined as greater than 0.5 second valve closure time after distal compression and release using duplex US in a non-weight-bearing limb with the patient in the standing position (83). Because valvular reflux is extremely common in the general population, determination of the impact of DVT treatments on its incidence and progression can be difficult. For this reason, duplex US examination of both limbs at baseline and at regular follow-up intervals is recommended. This enables characterization of the extent of residual thrombus and also enables use of the contralateral limb as an internal control. Plethysmography can quantify the volume of venous reflux but has largely been supplanted by duplex US in most centers (65).

Post-Thrombotic Syndrome.—The severity of PTS has historically been difficult to assess because many of its manifestations are not readily amenable to objective quantification. For this reason, many previous studies have reported only upon the most severe, objectively evaluable findings, such as the incidence of ulcer formation (84,85). However, this approach ignores the impact of lesser degrees of PTS on impairment of limb function and QOL. Fortunately, in recent years, several instruments have been developed to enable better determination of the presence and severity of post-thrombotic syndrome. The Venous Clinical Severity Score is one practical physician assessment method by which the severity of venous dysfunction in individual patients may be tracked (5). This measure is based on physician assessment of nine common stigmata of chronic venous disease. The Villalta Scale is an easy-to-apply measure that includes both patient-reported symptoms and physician-assessed signs of venous disease (43). In addition, a number of disease-specific questionnaire instruments have been developed to grade the severity of chronic venous disease and its impact on QOL, including the CIVIQ, Mathis, and VEINES-QOL/Sym scales (**Table 4** and Appendix 1) (44–49). The use of "homemade" nonvalidated questionnaire instruments for evaluating venous disease is discouraged now that other measures are available. However, efforts to develop new measures or further validate existing measures are strongly encouraged.

Health-Related Quality-of-Life.—In VTE patients, QOL can be adversely affected by late limb dysfunction and the late cardiopulmonary sequelae of PE and is a key outcome of interest. Because many aspects of the physical and psychological dysfunction caused by venous disease are difficult for a physician to assess, patient self-assessment questionnaires are commonly used to assess the impact of therapies on health-related QOL. Both disease-specific and general QOL questionnaires have been used in venous disease populations (44–51). General QOL measures can quantify the impact of therapy on overall well-being but can be insensitive to modest changes in the specific disease process. In other words, moderate changes in the severity of PTS are likely to be reflected in a disease-specific measure but might not affect general health-related QOL (86).

Assessment of Resource Utilization

Analysis of treatment expenses has traditionally been based on charges rather than costs to the hospital. Unfortunately, charges are arbitrary and true costs are often difficult to obtain (87). In addition, costs can vary depending on which party is incurring them (88,89). A rigorous analysis of DVT treatment costs should include the cost of all procedures, devices, and medications given; the cost of any in-patient treatment or intensive care unit care; the costs of immediate and long-term complications; and the costs of long-term monitoring and treatment.

RECOMMENDATIONS

Whenever possible, evaluation of the outcomes of endovascular DVT therapies should conform to the standards by which previous DVT therapies have been measured. Clinical DVT studies should quantify the impact of DVT therapies on clinically meaningful endpoints. Evaluation of surrogate outcome measures can help to determine whether the observed clinical outcomes occurred via the hypothesized mechanisms but cannot substitute for evaluation of the outcomes that are clinically relevant to patients.

It is recognized that certain types of clinical studies are performed to address narrow technical questions and are not intended to provide major assessments of clinical efficacy. For these "limited-scope" articles, authors may be exempted from the requirement to report on the long-term clinical endpoints described above. However, the authors must expressly state that the study goals are limited and must avoid drawing conclusions about parameters that would be most appropriately addressed by more detailed clinical outcomes evaluation. Clinical DVT studies that are not limited to specific technical questions should follow the recommendations presented here.

Authors must indicate what DVT outcomes measures were tracked sys-

tematically (ie, planned prospectively) and what measures were evaluated retrospectively. The study patients must be stratified into acute versus subacute versus chronic DVT and iliofemoral versus femoropopliteal versus calf vein DVT, and analyses of the groups must be performed separately and together. Because each limb is a discrete functional unit, efficacy outcomes pertaining to limb status should be reported on a per-limb basis. Safety outcomes, on the other hand, should be reported on a per-patient basis.

The incidences of proved PE and PE-related death for the entire patient population and for each treatment arm must be stated. Inclusion of the incidences of late pulmonary dysfunction, chronic pulmonary thromboembolism, and pulmonary hypertension is also recommended.

The proportions of treated limbs experiencing significant clinical improvement in swelling and pain must be reported. Objective measurement of limb swelling and pain using serial limb circumference measurements and validated pain scales is highly recommended. Description of the mean time to clinical improvement in each patient cohort is highly recommended. The proportion of limbs with progression of DVT must be reported. For studies including patients with phlegmasia cerulea dolens or venous gangrene, the limb salvage rate and amputation-free survival rate must be provided. The proportion of limbs in which technical success was achieved must be reported. It is recommended that investigators report the end-of-procedure patency of the suprarenal IVC, infrarenal IVC, common iliac vein, external iliac vein, common femoral vein, femoral vein, popliteal vein, deep femoral vein, and calf veins. For studies evaluating transluminal thrombus removal, estimation of the degree of thrombolysis using a venographic scoring system is highly recommended.

Because chronic venous disease may manifest itself over a long period of time after an episode of acute DVT, investigators should avoid making claims of "efficacy" for DVT treatment unless they can be supported by data indicating mid-term or long-term success. The primary patency, primary assisted patency, and secondary patency, early rethrombosis rate, late rethrombosis rate, and overall incidence of recurrent VTE must be reported. In reporting patency data, life-table analysis is highly recommended because it clearly indicates how many limbs have maintained success at each follow-up interval. Inclusion of duplex US data indicating the incidence of late valvular dysfunction is highly recommended. The VSDS is one useful method of quantifying the extent of reflux and obstruction.

The incidence and severity of PTS must be described using standardized measures. Use of at least one (and preferably more than one) of the following measures is required: VCSS (highly recommended), Villalta Scale, Venous Disability Score, or a disease-specific symptom/QOL questionnaire instrument. Use of a general QOL questionnaire is also recommended.

All complications must be tabulated and reported on a per-patient basis (Appendix 2). Complications must be categorized by outcome using the SIR classification system in which the most severe complication incurred is used (**Table 7**) (81). The proportion of patients who experience the following complications must be reported: procedure-related death, 30-day mortality and major morbidity, allergic reactions, sedation-related complications, intracranial bleeding, gastrointestinal bleeding, major or minor bleeding (include site, severity, and whether transfusion was needed), renal failure, procedure-related PE, venous rupture, and stent malposition/migration.

Table 7
SIR Classification of Complications by Outcome

Minor Complications
No therapy, no consequence
Nominal therapy, no consequence; includes overnight admission for observation only.
Major Complications
Require therapy, minor hospitalization (<48 hours)
Require major therapy, unplanned increase in level of care, prolonged hospitalization (>48 hours)
Permanent adverse sequelae
Death.

COMPARISON BETWEEN TREATMENT GROUPS

The randomized clinical trial is the criterion standard of clinical research and is the methodology of choice for determining the safety and efficacy of endovascular DVT treatments and for comparing them to other endovascular, surgical, and medical therapies (90). However, it is recognized that most studies will be of lesser methodologic rigor due to practical reasons such as cost, patient recruitment, and/or ethical considerations. Randomized trials should be performed in accordance with CONSORT guidelines (90).

Reports must indicate whether a study is single-center, multicenter, sponsored (if so, by whom), and if sponsored whether it was performed under the aegis of the United States Food and Drug Administration or another regulatory body. The institutional review board status must be provided. The study design, sample size, statistical power, and statistical analyses must be reported. Consultation with a statistician in the methodology of the study design and statistical analysis is recommended before starting the study.

Primary statistical analyses should be reported based on intent-to-treat and per-protocol analyses. With an intent-to-treat approach, subjects are analyzed with the group to which they were randomized whether or not they received the treatment or dropped out of the study. A per-protocol analysis considers only those patients who actually received the intended treatment.

Discussions of significance should incorporate the study design limitations. If the study conclusions are based on analysis of surrogate outcomes, they should be tempered accordingly. Authors should avoid drawing conclusions not clearly supported by the data; if alternate interpretations of the data are possible, they should be discussed.

CONCLUSION

Published studies on endovascular DVT treatments have been limited by nonstandardized reporting, lack of long-term follow-up, and use of surrogate outcomes measures. It is the purpose of these reporting standards to bring greater uniformity to endovascular DVT research reported in the radiology literature. A summary of the recommendations and requirements for reporting are provided in **Table 8**.

Table 8
Recommendations for Reporting Standards

Data	Req	HR	R
Population Description			
Demographic info	X		
Inclusion/exclusion criteria	X		
Method of treatment assignment	X		
% with DVT/PE/both/neither	X		
% with phlegmasia	X		
Method of DVT/PE diagnosis	X		
Stratify by symptom duration	X		
Risk factors/comorbidities	X		
Detailed risk factor description	X		
Previous VTE treatment	X		
Thresholds for laboratory values	X		
Define symptom status	X		
Limb circumference measurements		X	
Validated pain scales		X	
One: mean CEAP Class, VCSS score, VDS score, or disease-specific QOL measure	X		
More than one:		X	
General QOL instrument			X
Baseline anatomical extent of thrombus	X		
Baseline Duplex for reflux		X	
Treatment Description			
Originally intended treatment protocol	X		
Venous access site/method	X		
Below thrombus?	X		
Type and sequence of thrombus removal methods	X		
Route of delivery (systemic vs. flow vs. intrathrombus)	X		
Pharmacologic agent, dose, duration, route	X		
Lacing dose used	X		
Tourniquet system for flow-directed thrombolysis		X	
Mechanical thrombectomy device, model, method	X		
Device activation time		X	
Balloon maceration used	X		
Aspiration thrombectomy used	X		
Balloon thrombectomy used	X		
Venoplasty/stenting used (vessel, diameter, type)	X		
Filter used (indication, type, duration)	X		
Adjunctive surgical procedures	X		
Concomitant medical treatment and target range	X		
Outcomes Assessment			
Technical success	X		
Degree of thrombolysis (venographic assessment)			X
% with early symptom improvement	X		
Time to early symptom improvement		X	
% with progression of DVT	X		
Phlegmasia: limb salvage and amputation-free survival	X		
Proven PE and PE-related death*	X		
Suspected PE			X
Late pulmonary dysfunction			X
Chronic PE and pulmonary hypertension			X
Patency during follow-up/recurrent DVT*	X		
Recurrent VTE episodes*	X		
Duplex evaluation for valvular reflux*		X	
One: VCSS, VDS, Villalta scale, or	X		
More than one		X	
General QOL measure*	X		
Complications classified by SIR outcome scale	X		
48 hours after treatment	X		
30-day and overall	X		
Death	X		
Major bleeding	X		
Costs*			X
Analysis			
Study design	X		
IRB approval	X		
FDA regulatory status	X		
Statistical analysis	X		
Intent-to-treat	X		
Per-protocol		X	

* Not required for limited-scope articles. Req = required; HR = highly recommended; R = recommended.

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APPENDIX

Appendix 1. VEINES QOL/Sym Questionnaire

The VEINES questionnaire can be used to calculate two different summary scores. For each composite score, high scores indicate better clinical outcomes:

1. The VEINES–QOL summary score (based on 25 items) estimates the impact of chronic venous disease upon QOL. To compute: add point totals of the questions in each box except #2. Items in boxes #3, #6, and #7 must be reverse scored.

2. The VEINES-Sym summary score measures symptom severity. To compute: add point totals of the nine questions in box #1 and the question in box #7 (this item must be reverse scored).

The Questionnaire is available as a downloadable PDF document at www.jvir.org/cgi/reprint/17/3/417.

Appendix 2. SIR Complications Master List

Complication	Class
Abscess	Infectious/inflammatory
Angina/coronary reaction	Cardiac
Idiosyncratic reaction	Medication-related
Allergic/anaphylactoid reaction	Contrast-related
Arterial occlusion/thrombosis, puncture site	Vascular
Arterial occlusion/thrombosis, remote from puncture site	Vascular
Arteriovenous fistula	Vascular
Congestive heart failure	Cardiac
Contamination of pleural cavity (urine, bile, malignancy, empyema, other)	Respiratory/pulmonary
Device malfunction with adverse effect	Device-related
Death related to procedure	Death
Death unrelated to procedure (30-day mortality)	Death
Embolization, arterial	Vascular
Fluid/electrolyte imbalance	General nonvascular
Hematoma bleed, remote site	Vascular
Hematoma bleed at needle, device path: nonvascular procedure	Vascular
Hematoma bleed, puncture site: vascular procedure	Vascular
Incorrect drug	Medication-related
Incorrect dosage	Medication-related
Intimal injury/dissection	Vascular
Ischemia/infarction of tissue/organ	Vascular
Incorrect site of administration	Medication-related
Local infection	Infectious/inflammatory
Liver failure	General nonvascular
Migration	Device-related
Myocardial infarction	Cardiac
Malposition	Device-related
Nausea/vomiting	General nonvascular
Other (cardiac)	Cardiac
Other (contrast-related)	Contrast-related
Other (central nervous system complication)	Neurologic
Other (dose-dependent complication)	Contrast-related
Other (device related)	Device-related
Other (gastrointestinal)	General nonvascular
Other (general nonvascular)	General nonvascular
Other (hematologic)	General nonvascular
Other (infectious/inflammatory)	Infectious/inflammatory
Other (medication-related)	Medication-related
Other (neurologic)	Neurologic
Other pleural complication	Respiratory/pulmonary
Other (respiratory/pulmonary)	Respiratory/pulmonary
Other (vascular)	Vascular
Pancreatitis	Infectious/inflammatory
Pulmonary embolism	Respiratory/pulmonary
Pulmonary embolism	Vascular
Peritonitis	Infectious/inflammatory
Hypotension	Cardiac
Hypoxia	Respiratory/pulmonary
Pulmonary edema	Respiratory/pulmonary
Peripheral nervous system complication	Neurologic
Pneumothorax	Respiratory/pulmonary
Pseudoaneurysm	Vascular
Respiratory arrest	Respiratory/pulmonary
Renal failure	Contrast-related
Arrhythmia	Cardiac
Septicemia/bacteremia	Infectious/inflammatory
Seizure	Neurologic
Septic shock	Infectious/inflammatory
Stroke	Neurologic
Tissue extravasation	Contrast-related
Transient ischemic attack	Neurologic
Unintended perforation of hollow viscus	General nonvascular
Vascular perforation or rupture	Vascular
Vagal reaction	Cardiac
Vasospasm	Vascular
Venous occlusion/thrombosis, puncture site	Vascular
Venous occlusion/thrombosis, remote from puncture site	Vascular

INSTRUCTIONS
HOW TO ANSWER:
Answer every question by marking the answer as indicated. If you are unsure about how to answer a question, please give the best answer you can.

Below are some questions about your views about your legs. This information will help keep track of how you feel and how well you are able to do your usual activities.

1. During the past 4 weeks, how often have you had any of the following leg problems?

(check one box on each line)	**Every day**	**Several times a week**	**About once a week**	**Less than once a week**	**Never**
1. Heavy legs	1	2	3	4	5
2. Aching legs	1	2	3	4	5
3. Swelling	1	2	3	4	5
4. Night cramps	1	2	3	4	5
5. Heat or burning sensation	1	2	3	4	5
6. Restless legs	1	2	3	4	5
7. Throbbing	1	2	3	4	5
8. Itching	1	2	3	4	5
9. Tingling sensation (e.g.pins and needles)	1	2	3	4	5

2. At what time of day is your **leg problem** most intense ? *(check one)*

1 On waking
2 At mid-day
3 At the end of the day
4 During the night
5 At any time of day
6 Never

3. Compared to one year ago, how would you rate your **leg problem** in general now? *(check one)*

1 Much better now than one year ago
2 Somewhat better now than one year ago
3 About the same now as one year ago
4 Somewhat worse now than one year ago
5 Much worse now than one year ago
6 I did not have any leg problem last year

4. The following items are about activities that you might do in a typical day. Does your **leg problem** now limit you in these activities? If so, how much ?

(Check one box on each line)	I do not work	YES, Limited A Lot	YES, Limited A Little	NO, Not Limited At All
a. Daily activities at work	0	1	2	3
b. Daily activities at home (e.g. housework, ironing, doing odd jobs/repairs around the house, gardening, etc...)		1	2	3
c. Social or leisure activities in which you are standing for long periods (e.g. parties, weddings, taking public transportation, shopping, etc...)		1	2	3
d. Social or leisure activities in which you are sitting for long periods (e.g. going to the cinema or the theater, travelling, etc...)		1	2	3

5. During the past 4 weeks, have you had any of the following problems with your work or other regular daily activities as a result of your **leg problem**?

(check one box on each line)	YES	NO
a. Cut down the **amount of time** you spent on work or other activities	1	2
b. **Accomplished less** than you would like	1	2
c. Were limited in the **kind** of work or other activities	1	2
d. Had **difficulty** performing the work or other activities (for example, it took extra effort)	1	2

6. During the past 4 weeks, to what extent has your leg problem interfered with your normal social activities with family, friends, neighbors or groups? *(check one)*

1 Not at all
2 Slightly
3 Moderately
4 Quite a bit
5 Extremely

7. How much leg pain have you had during the past 4 weeks? *(check one)*

1 None
2 Very mild
3 Mild
4 Moderate
5 Severe
6 Very severe

8. These questions are about how you feel and how things have been with you during the past 4 weeks as a result of your **leg problem**. For each question, please give the one answer that comes closest to the way you have been feeling. How much of the time during the past 4 weeks -

	(check one box on each line)	All of the Time	Most of the Time	A Good Bit of the Time	Some of the Time	A Little of the Time	None of the Time
a.	Have you felt concerned about the appearance of your leg(s) ?	1	2	3	4	5	6
b.	Have you felt irritable ?	1	2	3	4	5	6
c.	Have you felt a burden to your family or friends ?	1	2	3	4	5	6
d.	Have you been worried about bumping into things ?	1	2	3	4	5	6
e.	Has the appearance of your leg(s) influenced your choice of clothing ?	1	2	3	4	5	6

Thank you for your help.
Please return this questionnaire to us by mail using the envelope provided or give it to your doctor.

Please write today's date: _____/_____/_____ *(day/month/year)*