

ACR Appropriateness Criteria[®]

Suspected Upper Extremity Deep Vein Thrombosis

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Upper-extremity venous thrombosis often presents as unilateral arm swelling. The differential diagnosis includes lesions compressing the veins and causing a functional venous obstruction, venous stenosis, an infection causing edema, obstruction of previously functioning lymphatics, or the absence of sufficient lymphatic channels to ensure effective drainage. The following recommendations are made with the understanding that venous disease, specifically venous thrombosis, is the primary diagnosis to be excluded or confirmed in a patient presenting with unilateral upper-extremity swelling. Contrast venography remains the best reference-standard diagnostic test for suspected upper-extremity acute venous thrombosis and may be needed whenever other noninvasive strategies fail to adequately image the upper-extremity veins. Duplex, color flow, and compression ultrasound have also established a clear role in evaluation of the more peripheral veins that are accessible to sonography. Gadolinium contrast-enhanced MRI is routinely used to evaluate the status of the central veins. Delayed CT venography can often be used to confirm or exclude more central vein venous thrombi, although substantial contrast loads are required.

The ACR Appropriateness Criteria[®] are evidence-based guidelines for specific clinical conditions that are reviewed every 2 years by a multidisciplinary expert panel. The guideline development and review include an extensive analysis of current medical literature from peer-reviewed journals and the application of a well-established consensus methodology (modified Delphi) to rate the appropriateness of imaging and treatment procedures by the panel. In those instances in which evidence is lacking or not definitive, expert opinion may be used to recommend imaging or treatment.

Key Words: Upper-extremity deep vein thrombosis, venography, ultrasound, magnetic resonance imaging, computed tomography, appropriateness criteria

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SUMMARY OF LITERATURE REVIEW

Introduction/Background

Upper-extremity venous thrombosis often presents as unilateral arm swelling. The differential diagnosis in-

cludes a mass lesion or other lesion compressing the veins and causing a functional venous obstruction, venous stenosis, or an infection causing edema [1]. Bilateral upper-extremity swelling may also be due to right-sided heart

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failure, although this is typically associated with generalized swelling, in contrast to central vein obstruction, which can cause swelling limited to the upper extremity and face [1].

Obstruction of previously functioning lymphatics or the absence of sufficient lymphatic channels to ensure effective drainage may also cause arm swelling. Lymphatic obstruction can be seen with infection such as cellulitis or can be secondary to invasion of the lymphatics by tumor. Absence of the lymphatics can be congenital or secondary to surgery, such as after a radical mastectomy [2].

The following recommendations are made with the understanding that venous disease, specifically venous thrombosis, is the primary diagnosis to be excluded or confirmed in a patient presenting with unilateral upper-extremity swelling.

Upper-Extremity Deep Vein Thrombosis (DVT)

Upper-extremity DVT can be associated with indwelling catheters [3-7], be idiopathic or posttraumatic [5,8], or be secondary to extrinsic compression syndrome ("effort thrombosis" or Paget-Schrötter disease) [5,9].

Upper-extremity DVT is commonly associated with the presence of indwelling central venous catheters [3,6,7,10-12]. The presence of a catheter, a foreign body, increases the likelihood of venous thrombosis by altering flow [1], causing damage to the endothelial lining of the vein, and serving as a site for platelet adherence [1]. The increased use of chronically indwelling catheters for hemodialysis, chemotherapy, or parenteral nutrition, often in a population that already has additional risk factors for venous thrombosis, has increased the incidence of upper-extremity DVT. As is the case with lower-extremity DVT, the likelihood of upper-extremity DVT increases with the presence of risk factors such as age, previous thrombophlebitis, postoperative state, hypercoagulability [3,4,8], heart failure [3], cancer [4-8,11,13], right-heart procedures, and intensive care unit admissions [7].

The location of the venous thrombosis is strongly linked to the clinical presentation. For example, head, neck, or bilateral upper-extremity swelling suggests a central process in the mediastinum [1] involving the superior vena cava or both subclavian and brachiocephalic systems [14]. Superficial thrombophlebitis is associated with local pain, induration, and, often, a palpable cord. It is rarely, if ever, associated with diffuse arm swelling [15]. Unilateral swelling indicates an obstructive process at the level of the brachiocephalic, subclavian, or axillary veins [14,15]. Deep vein thrombosis limited to the brachial veins need not be associated with swelling. Isolated jugular vein thrombosis is asymptomatic and rarely causes swelling. There may be a correlation between upper-extremity and lower-extremity DVT, and investigation of the lower extremities as well should be considered if an upper-extremity thrombus is found in the absence of a local cause [16].

Differentiating Causes of Upper-Extremity Swelling

The initial approach to a patient who presents with a swollen upper extremity is exclusion of venous thrombosis, because anticoagulation is typically required, and the underlying lesion may require a more aggressive intervention such as thrombolysis. Once the diagnosis of DVT is excluded, other etiologies may need to be evaluated. Combination of clinical features alone can be used to design a clinical prediction score for diagnosing upper-extremity DVT [17]. Blood tests can also be used to detect the presence of DVT. Plasma D-dimer is a degradation product of cross-linked fibrin that is elevated during thromboembolic events. The blood evaluation for plasma D-dimer in patients with suspected upper-extremity DVT is highly sensitive but not very specific [18]. It is also unreliable to diagnose recurrent DVT or alternative conditions that mimic DVT and is unable to assess the location and extent of the venous thrombus, which is critical for proper therapeutic management of DVT [19].

Imaging is often required for definite exclusion of DVT and to document its location and extent. Different imaging techniques that can be used to achieve the diagnosis include noninvasive tests such as radionuclide venography, ultrasound, MRI, CT, and venography. Other techniques, such as photoplethysmography, might also prove useful [20] (see Variant 1).

Chest Radiography

Because of the broad differential diagnoses of upper-extremity swelling, chest radiography may identify a mass lesion responsible for central venous obstruction or help confirm the presence and location of wires, catheters, or a retained wire or catheter fragment. Rare osseous entities that might be associated with extrinsic compression syndromes, such as a cervical rib, would also be detected.

Radionuclide Imaging, Flow Studies

Radionuclide studies can confirm upper-extremity venous obstruction. The diagnostic criteria include failure to visualize one or more of the main venous segments (axillary, subclavian, brachiocephalic, or superior vena cava) and visualization of collateral venous channels. This test is typically not able to differentiate intrinsic venous thrombosis from extrinsic compression [2,21-23].

X-Ray Venography

This is the "reference standard" [24] examination for evaluating the upper-extremity veins. The examination carries the risks associated with the injection of an iodinated contrast agent [24,25]. Patient tolerance has been improved, and the risks of adverse events have been reduced with low-osmolar contrast agents. Direct evidence of venous thrombus is based on the visualization of a filling defect in the vein. Less specific findings for venous

Variant 1. Suspected upper-extremity deep vein thrombosis

Radiologic Procedure	Rating	Comments	Relative Radiation Level
Ultrasound upper extremity(ies) with Doppler	9	Standard for arm veins. Other modalities are required for evaluating central veins.	○
X-ray chest	8	Simple, low-cost evaluation of lines, mediastinal contours, and cervical ribs.	☼
MRA (venography) chest (noncoronary) without and with contrast	7	Asymptomatic side injection is preferred. For central veins. See statement regarding contrast in text under “Anticipated Exceptions.”	○
MRA (venography) chest (noncoronary) without contrast	7	Can be performed when contrast is contraindicated.	○
X-ray venography upper extremity(ies) and SVC	7	Although this is the gold standard, it generally reserved for inconclusive noninvasive studies.	☼☼☼
CTA (venography) chest (noncoronary) with contrast	7	Asymptomatic side injection is preferred. Alternative to MR venography for central veins.	☼☼☼☼
Radionuclide venography upper extremity(ies) and chest	3	Largely supplanted. Limited use for central veins when CT and MR venography are both contraindicated.	☼☼☼

Note: Rating scale: 1, 2, and 3 = usually not appropriate; 4, 5, and 6 = may be appropriate; 7, 8, and 9 = usually appropriate. CTA = CT angiography; MRA = MR angiography; SVC = superior vena cava.

thrombus include abrupt contrast cutoff, absence of contrast filling, or the presence of collateral channels [26]. Venography can identify fixed venous stenoses and, with upper-extremity maneuvers (abduction), can identify extrinsic venous compression. Asymptomatic or minimally symptomatic venous compression with arm abduction should be treated with caution, as this finding can be made in a substantial number of normal individuals. Venography can also identify recurrent acute venous thrombus in patients with histories of venous thrombus. Despite its widespread acceptance as a reference standard on the basis of extension of evidence associated with lower-extremity DVT, there are few clinical trials supporting its use.

Venous Ultrasound

This relatively inexpensive test can exclude DVT and help identify a proximal venous obstruction. It is noninvasive, can be performed at the patient's bedside, and can be used for serial evaluation. Diagnostic criteria for direct evidence of thrombus, as in the lower extremity, include loss of compression of imaged vein walls when pressure is applied on the skin during real-time imaging, and visualization of echogenic material in the vein. Indirect evidence of thrombus includes altered blood flow patterns [8,25-29]. Loss of compressibility is consistent with acute DVT but can also occur in the presence of chronic venous thrombosis [8,26]. This can be used for peripheral veins such as jugular, axillary, basilic, cephalic, and brachial veins. Compression cannot be used to evaluate subclavian or more central veins, because bony structures prevent visualization or compression of the veins.

A full examination also includes evaluation of the Doppler velocity profiles obtained from blood in the major veins and color flow Doppler imaging. Reduction in Doppler velocity changes due to cardiac pulsa-

tility are reliable indicators of central venous obstruction [12,29,30]. In addition, respiratory maneuvers such as rapid inspiration or “sniffing” should cause the walls of the subclavian veins to collapse [24,30,31]. Impairment of this collapse (which is related to rapid venous emptying) also indicates a central obstructive process [10,29,30]. However, a central thrombus will cause the same alterations in blood flow as a mass encasing or compressing the central (superior vena cava, brachiocephalic) veins or a benign stricture. Color flow imaging can be used to image the presence or absence of flow within the vein and is useful in evaluating venous segments for which compression maneuvers cannot be applied (eg, to the central subclavian vein) [8,10,30], although a study has suggested that if only blood flow abnormalities are seen, conventional venography may be necessary [8].

Grayscale imaging can be used to identify an echogenic thrombus. However, acute hypoechoic thrombi may be missed using grayscale imaging alone. Adjunctive use of color flow images can help confirm the presence or absence of hypoechoic thrombus and can also help determine if a clot is obstructive or partially obstructive. Correlative studies between ultrasound and venography show diagnostic sensitivities and specificities > 80% [5,8,10,12,24-26,29,31-33].

MRI

Approaches to venous imaging using MRI include black-blood and flow-based or contrast-enhanced bright-blood techniques [34]. Black-blood techniques include conventional T1 or T2 spin-echo [28,35] or fast spin-echo imaging. However, the black-blood effect on routine spin-echo imaging may not be consistent, and newer double inversion-recovery techniques provide more reli-

able black-blood imaging [34]. Using black-blood imaging, the presence of thrombus is inferred from focal high signal, often with enlargement, of the involved vein, but it must be differentiated from a variety of flow artifacts [35]. The high signal in thrombus on T1 imaging decreases after 6 months, and the technique is less useful for chronic thrombus [36].

Techniques for flow-based bright-blood MR venography (MRV) include time-of-flight (TOF) [34,37,38] and phase contrast [34,35]. For venous imaging, TOF is limited to a 2-D implementation because of signal saturation of slow flow [39]. Vessels with primarily in-plane flow are more difficult to image, because of saturation [39]; 2-D TOF is thus most useful in the axial plane to image flow in the jugular veins, right brachiocephalic vein, and superior vena cava, which are oriented primarily in the superior-inferior direction. Time-of-flight venography can be used to image the subclavian vein, but more time-consuming sagittal acquisitions are preferred because of the direction of flow, and breathing artifacts may also impair imaging quality [4,39,40]. Phase contrast has not been widely used for upper-extremity venography, because of the slow flows that must be detected [39]. Recently, balanced gradient-echo (steady-state free precession) and cardiac-gated 3-D fast spin-echo techniques have been implemented for noncontrast MR vessel imaging. Although these techniques have not been evaluated for chest venography, they seem promising [39,41,42]. Balanced gradient-echo images alone are insensitive for detecting central venous thrombus [43], partly because of the variable signal intensity of thrombus over time, as acute thrombus is relatively isointense to blood with such sequence. Cardiac-gated 3-D fast spin-echo techniques can help differentiate transient flow artifacts from true filling defects that persist over the cardiac cycle.

Contrast-enhanced MRV [37,44,45] can also be used by implementing 2-D or 3-D T1 gradient-echo images with fat saturation after the administration of a single or a double dose of MR contrast [39]. Typically, venous imaging is carried out after MR arteriography by simply imaging out into the venous or equilibrium phases of contrast distribution [34,39]. Fibrin-specific MR contrast agents have also been developed that can further enhance all thrombi and even detect thrombi not readily visible in precontrast imaging [46]. New time-resolved imaging allows visualization of flow dynamics and may decrease required contrast volume and acquisition time and improve specificity [47]. It has found use in protocols for whole-body venography [48] and was shown to produce images of comparable diagnostic quality but lower specificity compared with conventional MRV [49] in the assessment of central thoracic veins. It might eventually be used to safely image patients with poor renal function, but further study is required.

The advantages of MRV are primarily for central ve-

nous evaluation, as the central veins cannot be imaged directly using ultrasound. For imaging the arm itself, ultrasound or even x-ray venography is preferred. Magnetic resonance venography of the arm is rendered more difficult by its placement at the periphery of the magnetic field or the requirement to maintain the arm motionless over the head. Magnetic resonance imaging has a strong ability to delineate extravascular anatomy. It can be used to identify alternative diagnoses that mimic DVT and identify sources of extrinsic venous compression that may be an underlying cause for DVT. Thus, MRV protocols often include standard MRI sequences such as T1-weighted (spin-echo, gradient return echo) and T2-weighted (fast spin-echo) sequences to assess the anatomy surrounding the vessels. Studies so far specifically comparing MRV with venography have been mixed, with some work showing MRV to be as effective as venography [38,45] but other work showing its limitations [28,35,37]. A recent meta-analysis found MRV to have both high sensitivity and high specificity [50], although the study was not focusing on the upper extremities.

CT

Computed tomography can be used to determine the presence of centrally located thrombi or stenoses within the jugular veins [51,52], the brachiocephalic veins [53,54], and the superior vena cava [53]. The presence of an extrinsic process causing venous obstruction of the venous channels can also be determined [55]. Computed tomography is the main imaging modality for staging neoplastic involvement in the mediastinum and axillae, which can include vascular invasion or compression. Perivascular inflammatory changes around chronic thrombi can also be detected by CT [56]. Delayed imaging at 90 to 120 seconds can permit evaluation of the central veins. It is important to administer large doses of contrast (up to 150 cm³) to ensure adequate venous opacification. New techniques involving dual injections of contrast have been developed for CT venography and look promising [57]. No large series have looked at the diagnostic accuracy of this technique for diagnosing upper-extremity venous thrombosis, although extensive experience is accumulating with lower-extremity venous thrombosis. One small series showed that the performance of CT venography is similar to that of conventional venography in the thoracic and upper-extremity veins and that it evaluates the central extent of obstruction more effectively [55].

SUMMARY

- Despite the availability of noninvasive imaging techniques, contrast venography remains the best reference standard diagnostic test for suspected upper-extremity acute venous thrombosis.

- Contrast venography may be needed whenever other noninvasive strategies fail to adequately image the upper-extremity veins. Additionally, because venography is the first step in direct catheter-based thrombolysis, in situations such as acute upper-extremity DVT in which the likelihood of percutaneous thrombectomy or thrombolysis is high, it is sensible to proceed directly to venography.
- Duplex, color flow, and compression ultrasound have also established a clear role in evaluation of the more peripheral veins that are accessible to sonography.
- Gadolinium contrast–enhanced MRI is routinely used to evaluate the status of the central veins. Unfortunately, despite its widespread clinical use, there are few validation studies of this technique compared with the extensive literature on contrast venography. The recognition of gadolinium as a cause of nephrogenic systemic fibrosis has increased interest in noncontrast MRV, but validation of these techniques in the chest remains an issue.
- Delayed CT venography can often be used to confirm or exclude more central vein venous thrombi, although substantial contrast loads are required. As in the case of MRV, there are few correlative studies justifying this approach.

ANTICIPATED EXCEPTIONS

Nephrogenic systemic fibrosis is a disorder with a scleroderma-like presentation and a spectrum of manifestations that can range from limited clinical sequelae to fatality. It seems to be related to both underlying severe renal dysfunction and the administration of gadolinium-based contrast agents. It has occurred primarily in patients on dialysis, rarely in patients with very limited glomerular filtration rates (ie, <30 mL/min/1.73 m²), and almost never in other patients. There is growing literature regarding nephrogenic systemic fibrosis. Although some controversy and lack of clarity remain, there is a consensus that it is advisable to avoid all gadolinium-based contrast agents in dialysis-dependent patients unless the possible benefits clearly outweigh the risk and to limit the type and amount in patients with estimated glomerular filtration rates < 30 mL/min/1.73 m². For more information, please see the ACR's *Manual on Contrast Media* [58].

RELATIVE RADIATION LEVEL INFORMATION

Potential adverse health effects associated with radiation exposure are an important factor to consider when selecting the appropriate imaging procedure. Because there is a wide range of radiation exposures associated with different diagnostic procedures, a relative radiation level indication has been included for each imaging examination. The relative radiation levels are based on effective dose, which is a radiation dose quantity that is used to estimate population total radiation risk associated with an imag-

Table 1. Relative radiation level designations

Relative Radiation Level	Adult Effective Dose Estimate Range (mSv)	Pediatric Effective Dose Estimate Range (mSv)
○	0	0
⊙	<0.1	<0.03
⊛	0.1-1	0.03-0.3
⊞	1-10	0.3-3
⊟	10-30	3-10
⊠	30-100	10-30

Note: Relative radiation level assignments for some of the examinations cannot be made, because the actual patient doses in these procedures vary as a function of a number of factors (eg, region of the body exposed to ionizing radiation, the imaging guidance that is used). The relative radiation levels for these examinations are designated as not specified.

ing procedure. Patients in the pediatric age group are at inherently higher risk from exposure, both because of organ sensitivity and longer life expectancy (relevant to the long latency that appears to accompany radiation exposure). For these reasons, the relative radiation level dose estimate ranges for pediatric examinations are lower compared with those specified for adults (Table 1). Additional information regarding radiation dose assessment for imaging examinations can be found in *ACR Appropriateness Criteria*[®]: *Radiation Dose Assessment Introduction* [59].

For additional information on ACR Appropriateness Criteria, refer to <http://www.acr.org/ac>.

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