Treating the DVO Picture: Significance of Imaging in Relation to the Complaints of the Patient

A structured approach to the imaging workup for deep venous obstruction of the lower limbs.

BY VINCENT G. HELYAR, MBBS, MSc, FRCR, EBIR; STEPHEN A. BLACK, MD, FRCS(Ed), FEBVS; AND NARAYAN KARUNANITHY, MBBS, MRCS, FRCR, EBIR

Deep venous obstruction (DVO) is common and consists of acute (deep vein thrombosis [DVT]) and chronic (postthrombotic syndrome [PTS]) entities. DVT is often isolated to the thigh and calf veins, but approximately 8% extend above the inguinal ligament.[1] Although infrainguinal DVT is managed with anticoagulation only, there is evidence indicating that treating suprainguinal (iliofemoral) DVT with catheter-directed thrombolysis (CDT) and stenting of any underlying obstructive lesion improves long-term outcomes by reducing the incidence of PTS.[2,3] In patients considered for CDT, imaging provides essential information that helps in case selection and in individualizing the interventional strategy.

PTS is a debilitating condition with an incidence rate up to 75% after symptomatic lower limb DVT.[4] PTS is associated with a myriad of symptoms, including skin pigmentation, venous ectasia, pain, chronic edema, and ulceration. The symptoms negatively affect quality of life and are associated with a significant economic burden. The pathogenesis of PTS is complex. It is thought to arise from a combination of venous outflow obstruction and an inflammatory reaction affecting the vessel wall and valves leading to reflux. An increasing number of patients are considered for venous reconstruction, and a spectrum of interventional strategies are now available. Reliable and detailed preprocedural imaging assessment allows the development of a tailored treatment plan factoring in individual patient symptoms and needs. These treatment strategies are typically devised in a multidisciplinary team composed of hematology, vascular surgery, and interventional radiology.

The imaging workup of patients with suspected DVO may involve various modalities including color Doppler ultrasound (CDUS), CT venography (CTV), magnetic resonance venography (MRV), intravenous digital subtraction angiography, and intravascular ultrasound (IVUS). This article discusses the role and relative merits of each of these imaging modalities.

IMAGING FOR ACUTE DVT

CDUS is the first-line imaging modality used for diagnosing infrainguinal (calf and thigh) acute DVT and has a high sensitivity and specificity.[5] The accuracy of CDUS diminishes when assessing the suprainguinal veins due to bowel interposition, obesity, and edema. Acutely obstructed veins are distended, noncompressible, and there is hyperechoic intraluminal thrombus present. The absence of flow on CDUS with augmentation is an additional feature. Patients with suprainguinal thrombus extension would generally be considered for CDT if they fulfill the inclusion and exclusion criteria outlined in Table 1.[6] In patients considered for CDT, there are significant imaging findings that can influence the management strategy adopted, including:

TABLE 1. INCLUSION AND EXCLUSION CRITERIA FOR THE INITIATION OF CATHETER-DIRECTED THROMBOLYSIS IN PATIENTS WITH ACUTE ILIOFEMORAL DVT[6]	
Inclusion Criteria	**Exclusion Criteria**
• Symptoms (duration < 14 d) • Good functional status • Life expectancy of ≥ 1 y	• High risk of bleeding • Hemorrhagic stroke • Head trauma/brain surgery < 6 mo • Intracranial neoplasm • Active bleeding diathesis • Recent major surgery, trauma, or bleeding • Recent ocular surgery • Known right-left cardiopulmonary shunt

- **The extent of proximal (upper) thrombus extension.** Typically, there is no thrombus extension into the inferior vena cava (IVC) with left leg iliofemoral DVT because of May-Thurner compression preventing proximal thrombus propagation. However, when IVC extension of thrombus is seen, there are two important considerations. First, as there is a large volume of thrombus, a pharmacomechanical strategy may be preferred (using a device, such as the Angiojet [Boston Scientific Corporation]) over purely pharmacologic lysis. Second, a caval filter may be indicated due to the increased risk of pulmonary emboli associated with IVC thrombosis. At our institution, we do not routinely insert caval filters in patients undergoing CDT.
- **The presence of variant venous anatomy.** Variant deep venous anatomy such as IVC atresia or duplicated IVC is relatively common. Consideration of how the anomaly is to be managed is pertinent before starting thrombolysis (eg, stenting of an atretic IVC).
- **Unexpected underlying pathology.** In a small proportion of patients, the iliofemoral DVT may have been provoked. Figure 1 shows a left iliofemoral DVT occurring in a patient with previously undiagnosed metastatic carcinoma of the pancreas. Knowledge of this underlying abnormality may influence the decision to proceed to CDT.
- **Extrinsic venous compression.** Increasingly extrinsic venous compression, particularly May-Thurner compression, is recognized, and the prevalence is estimated to be > 80%. Patients with iliofemoral DVT up to an extrinsic compression point would undergo clot lysis followed invariably by stenting of the extrinsic compression if it is deemed to be causing a significant stenosis.

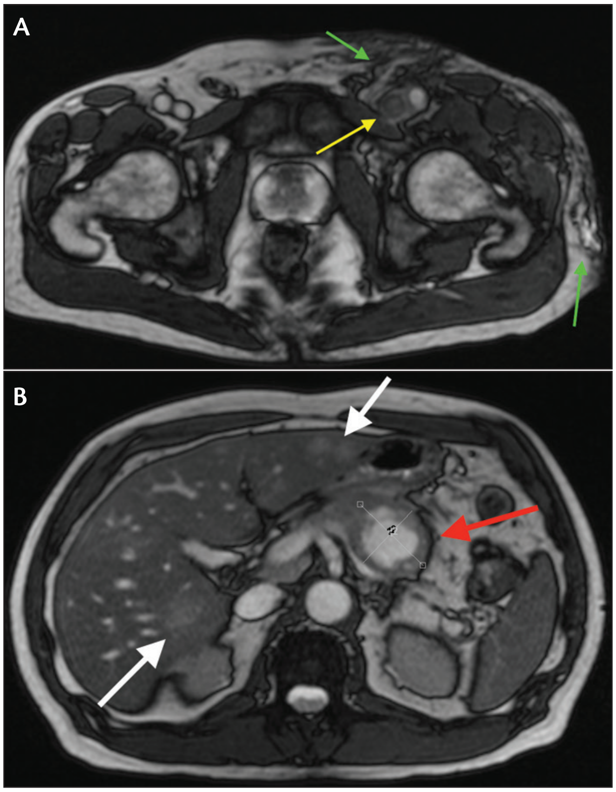

Figure 1. Balanced steady-state MRV demonstrates distended left common femoral vein with low signal occlusive thrombus with perivenous (A) (yellow arrow) and subcutaneous (A) (green arrows) edema, irregular thick-walled cystic lesion within the body of the pancreas—cystadenocarcinoma (B) (red arrow), and multiple liver metastases (B) (white arrow).

- **Thrombus age.** Clinical symptoms may not always correlate with true thrombus age. As CDT is most effective with acute (< 14 days) thrombus, being able to reliably predict thrombus age allows only those patients most likely to benefit to be included for treatment.

MRV (with or without exogenous contrast administration) and CTV techniques have been refined over recent years to address these questions. At our institution, noncontrast MRV (balance steady-state free precession [SSFP]) is preferred because it provides a "flow independent" means of assessing the deep venous system, is quick (typically 10–12 min of acquisition time), and does not involve exposure to ionizing radiation (compared with CTV) or exogenous contrast agent (compared with CTV and contrast-enhanced MRV). Acute DVT is depicted as intraluminal low signal within a distended vein with associated perivenous and subcutaneous edema (Figure 1). Various studies have demonstrated sequences of this type to be highly sensitive (100%) and specific (98.5%) for characterizing venous anatomy.[7]

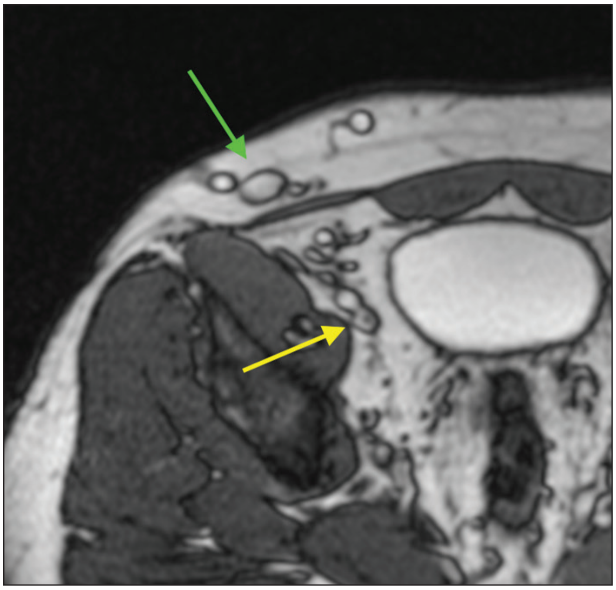

Figure 2. Small-caliber right external iliac vein with post-thrombotic webs (yellow arrow) and established collateral veins within the anterior abdominal wall (green arrow) indicate chronic venous outflow obstruction.

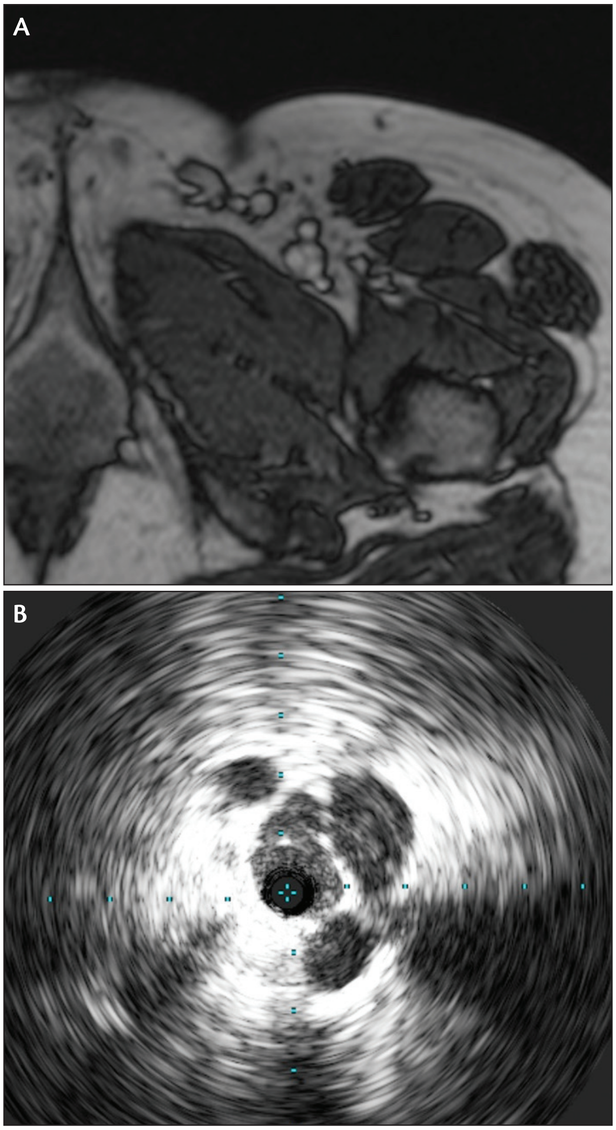

Figure 3. Balanced steady-state MRV demonstrates Mercedes Benz–shaped postthrombotic webs within the left common femoral vein (A) and IVUS correlation in the same segment of vein (B).

Predicting the significance of extrinsic compression can be very difficult on all forms of cross-sectional imaging, IVUS provides by far the most accurate indication of significant compression lesions and their extent.

There are morphologic features on MRV that may indicate thrombus age. The presence of perivenous and subcutaneous edema is more commonly seen with acute thrombus and a small-caliber vein with postthrombotic webs and adjacent collateral veins indicate chronic thrombus (Figure 2). Recent experimental data suggest that it may also be possible to age thrombus reliably with functional MRI techniques that interrogate the protein content of thrombus. These techniques may help to identify patients who will benefit most from lytic therapy.[8]

Contrast-enhanced MRV may also be performed but is associated with longer scan times. CTV remains a popular choice for imaging patients with suspected acute DVO. It is widely available, well tolerated, and provides detailed information about the venous anatomy. The radiation burden (< 3 mSv with the latest techniques) is a relative disadvantage, particularly in younger patients. The need to administer intravenous contrast medium is a further disadvantage, due to the small associated risk of nephrotoxicity. A CTV is typically performed following an injection of contrast medium into a peripheral upper limb vein with image acquisition performed 120 to 150 seconds after contrast injection. The so called direct CTV may also be performed following an injection of contract media into a lower limb or foot vein. However, venous cannulation in the foot can be time-consuming and difficult in this patient cohort. Features of acute venous obstruction on CTV are an enlarged vein filled with low attenuation material and an enhancing wall. Potential drawbacks are slow-moving blood and contrast mixing, which may give a false impression of thrombosis.

IMAGING FOR PTS

The essential role of imaging in the workup of PTS is to unravel the complex relationship of venous outflow obstruction and venous reflux by establishing the extent and severity of venous outflow obstruction. This allows patients that would benefit from deep venous reconstruction to be identified.

Features of chronic venous obstruction in the infrainguinal veins are readily demonstrated with CDUS. A small-caliber vein with impaired flow suggests stenosis; failure to visualize the vein may suggest chronic occlusion. Postthrombotic webs may also be seen within recanalized veins. In addition, reflux within the superficial and deep venous systems is demonstrated.

Balanced SSFP MRV is routinely performed at our institution for the workup of patients with suspected chronic venous outflow obstruction. Features of venous outflow obstruction are stenosis, extrinsic compression, and postthrombotic webs (Figure 3). The presence of collateral veins is also an extremely useful sign. These findings are mirrored on CTV, although postthrombotic webs are not clearly depicted. However, the hemodynamic significance at typical extrinsic compression points (eg, left common iliac vein between the right common iliac artery and vertebral body, May-Thurner/Cockett syndrome) may be difficult to predict on MRV or CTV. IVUS is a useful adjunct that provides a real-time, 360˚, inside-out view of the vessel and is helpful for evaluating these extrinsic compression points (Figure 4). Given the 360˚ nature of the IVUS image, stenoses are depicted more accurately than venography.[9] The real-time nature of IVUS also gives an indication of vessel caliber change during respiration or the Valsalva maneuver, providing valuable visual assessment of the hemodynamic properties not demonstrated on MRV/CTV. This may be particularly useful to determine the relative significance of nonthrombotic vascular lesions. Defining a precise cutoff for a stenosis has proven difficult in the veins; however, most physicians suggest stenosis > 50% may be sufficient to cause significant symptoms.[10]

Interventional deep venous reconstruction (I-DVR) is usually indicated in patients with significant PTS and proven suprainguinal venous outflow obstruction.[6] When considering I-DVR, establishing the extent of venous outflow obstruction is vital, especially the degree of IVC and common femoral vein involvement. IVC involvement up to the hepatic vein confluence can be treated effectively with stent placement, but consideration will need to be given to the configuration of stents to be deployed and often necessitates bilateral iliac vein reconstruction. Involvement of the common femoral vein, and especially the confluence of the femoral and deep femoral veins, poses a much more complex problem. When there is stenosis or postthrombotic web at the confluence, there is a high probability that the inflow into any iliac vein reconstruction will be suboptimal. In these patients, there is an increased risk of early stent thrombosis, and patients must be counseled accordingly. Some care teams therefore advocate performing endophlebectomy and arteriovenous fistula to optimize the inflow for this group. Preprocedure cross-sectional imaging (MRV or CTV) and IVUS are both essential imaging tools for diagnosing confluence disease and particularly subtle postthrombotic webs. Identifying these allows for an informed decision to be made about the merits and risks of I-DVR for addressing the complaints of the individual patient and whether I-DVR is advisable in the first place. Although balanced SSFP MRV allows for the depiction of even subtle postthrombotic webs, IVUS remains the gold standard for identifying these. CTV is relatively poor at depicting postthrombotic webs, and there is a real danger that lesion extent will be underrecognized if there is complete reliance on this modality alone.

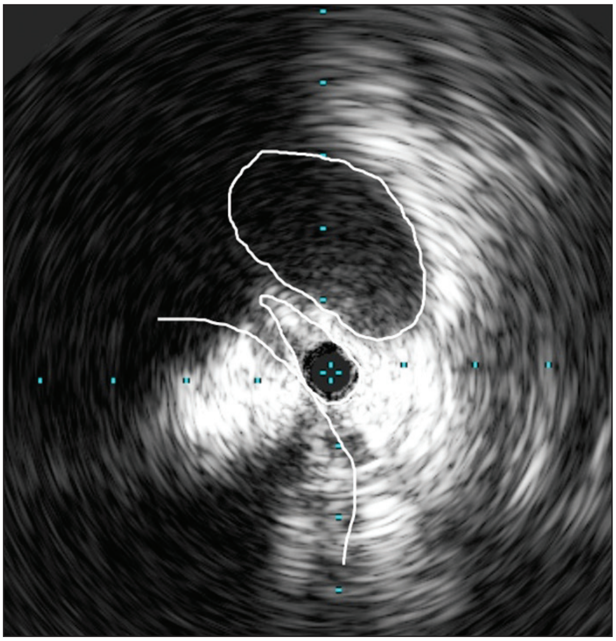

Figure 4. IVUS image of the left common iliac vein that is extrinsically compressed between the right common iliac artery and the vertebral body.

The spectrum and availability of advanced imaging modalities like MRV, CTV, and IVUS means that there is a risk that imaging findings are given a high impact in the decision-making process. Overtreatment (eg, stenting of the common iliac vein when there is a nonthrombotic vascular lesion, which on IVUS demonstrates > 50% compression) is a serious danger. I-DVR is a relatively young field, and long-term outcomes and complications are not known.

CONCLUSION

Noninvasive imaging (eg, CDUS, MRV, CTV) provides essential information regarding the extent and severity of acute and chronic DVO that, taken in context with a patient's clinical and hematologic findings, helps to tailor individual treatment strategies. In the event of equivocal imaging, misalignment of clinical findings to imaging, previous iliofemoral or caval stenting, or other complexities (eg, anomalous anatomy), IVUS provides extremely valuable synergistic information that can help unravel the complex relationship between the possible underlying pathologies and guide treatment decisions. Treatment plans should be devised in the setting of a multidisciplinary meeting and must be driven by the patient's clinical context. Treating incidental (ie, nonsymptomatic) venous compression is of dubious benefit to the patient and is likely to result in excess morbidity and possible litigation. ■

1. Casey ET, Murad MH, Zumaeta-Garcia M, et al. Treatment of acute iliofemoral deep vein thrombosis. J Vasc Surg. 2012;55:1463-1473.
2. Watson L, Broderick C, Armon MP. Thrombolysis for acute deep vein thrombosis. Cochrane Database Syst Rev. 2016;11:CD002783.
3. Haig Y, Enden T, Grøtta O, et al. Postthrombotic syndrome after catheter-directed thrombolysis for deep vein thrombosis (CaVenT): 5-year follow-up results of an open-label, randomised controlled trial. Lancet Haematol. 2016;3:e64-e71.
4. Prandoni P, Kahn SR. Postthrombotic syndrome: prevalence, prognostication and need for progress. Br J Haematol. 2009;145:286-295.
5. Goodacre S, Sampson F, Thomas S, et al. A systematic review and meta-analysis of the diagnostic accuracy of ultrasonography for deep vein thrombosis. BMC Med Imaging. 2005;5:6.
6. National Institute for Health and Care Excellence. Clinical guideline (CG144)—Venous thromboembolic disease: diagnosis, management and thrombophilia testing. NICE Web site. www.nice.org.uk/guidance/cg144. Accessed June 13, 2017.
7. Lindquist C, Karlicki F, Lawrence P, et al. Utility of balanced steady state free precession MR venography in the diagnosis of lower extremity deep vein thrombosis. AJR Am J Roentgenol. 2010;194,1357-1364.
8. Andia M, Saha P, Jenkins J, et al. Fibrin-targeted magnetic resonance imaging allows in vivo quantification of thrombus fibrin content and identifies thrombi amenable for thrombolysis. Arterioscler Thromb Vasc Biol. 2014;34:1193-1198.
9. Neglén P, Raju S. Balloon dilation and stenting of chronic iliac vein obstruction: technical aspects and early clinical outcome. J Endovasc Ther. 2000;7:79-91.
10. McLafferty, R. The role of intravascular ultrasound in venous thromboembolism. Semin Intervent Radiol. 2012; 29:10-15.

Vincent G. Helyar, MBBS, MSc, FRCR, EBIR
Interventional Radiology Fellow
Guy's and St Thomas' NHS Foundation Trust
London, United Kingdom
Disclosures: None.

Stephen A. Black, MD, FRCS(Ed), FEBVS
Consultant Vascular Surgeon
Guy's and St Thomas' NHS Foundation Trust
London, United Kingdom
Disclosures: None.

Narayan Karunanithy, MBBS, MRCS, FRCR, EBIR
Consultant Interventional Radiologist
Guy's and St Thomas' NHS Foundation Trust
London, United Kingdom
+44 207 188 5463; narayan.karunanithy@gstt.nhs.uk
Disclosures: None.