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VENOUS IMAGING

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Introduction

"As, year by year there is an increase in the number of patients operated upon in a more rational matter, so the demands upon X-ray examination of these patients have also risen. Under these circumstances it seems to be of great importance that a method of phlebography be worked out that would be as far as possible informative and reliable and, at the same time, simple of performance."[1] Today these words remain as true as when they were first written in 1960 by the "godfather" of venography, Gunnar Bauer. The modalities available to image the venous system are abundant: conventional direct venography (CV), duplex ultrasound (DUS), intravascular ultrasound (IVUS), magnetic resonance (MRV) venography, and computed tomography (CTV) venography. Both MRV and CTV have revolutionized the way we look at the venous system as they readily and reliably demonstrate the structures in question. Both allow for large fields-of-view (FOV), with cross-sectional images that provide superb soft tissue detail and levels of contrast that permit clear delineation between veins and adjacent structures. This is very valuable in identifying extra- or intraluminal filling defects that impact venous structures. Their usefulness becomes even more evident as vascular interventionalists continue to implant more and more devices in the venous system. We start to understand that sizing and visualization of these devices is as important in the venous system as it is in the arterial. The impact of respiration, cardiac function, and Valsalva on the central venous structures is quite pronounced and can profoundly affect the interpretation of venous anatomy. One must be cognizant of this fact when interpreting a diagnostic study. As much as possible, the aim should be in the direction of less-invasive imaging. This can be successfully achieved with MRV, CTV, and DUS, but each modality has its strengths and weaknesses. We will discuss the relevance of these studies as they apply to the most important clinical applications for venous disease.

Venous Thromboembolic Disease (Vte)

In 1856, German physician Rudolph Virchow published his description of the relationship between dislodged extremity venous thrombi migrating and lodging in the pulmonary arteries. The significance of these disorders is reflected in their incidence today, with 2.5 million cases of fatal and nonfatal venous thrombosis and over 500,000 pulmonary emboli (PE) occurring annually in the United States.[2, 3] The etiology of most venous thromboses can be attributed to three mechanisms: vessel wall injury, stasis of flow, and hypercoagulability, otherwise known as Virchow's triad.

The ability to rapidly and accurately identify and treat any disease process often depends not only on the clinical assessment of patients but also on selecting the most appropriate diagnostic test to confirm this assessment. For many years, the gold standard for diagnosing both acute and chronic venous thrombosis was contrast venography (CV). Equivocal duplex exams, pre- and post-lysis assessment, preoperative planning in complex venous reconstruction, and assessment of central venous obstruction all remain indications for the performance of CV (Figure 1).

First described in 1923, CV evolved into a standard of care for the diagnosis of deep venous thrombosis (DVT)

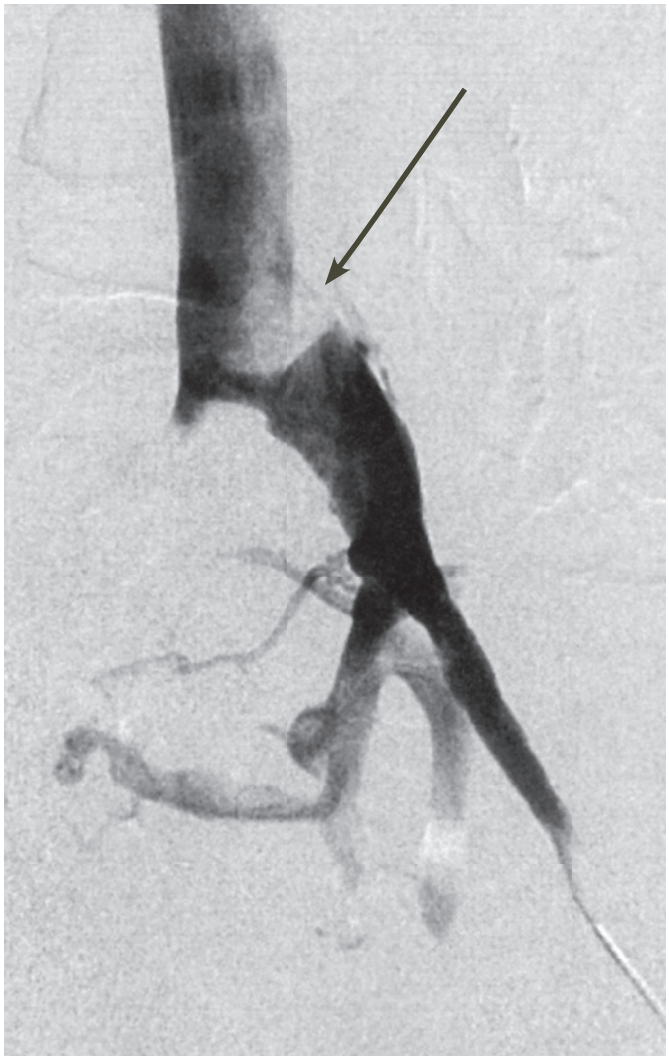

Figure 1. Contrast venography demonstrates left common iliac vein stenosis (arrow) due to compression by right common iliac artery or May-Thurner syndrome

in the 1960s. The technique for ascending venography has been well described in the literature and is used primarily to define venous anatomy. The procedure involves the instillation of contrast into a superficial vein on the dorsum of the foot and, with a tourniquet placed above the ankle to force contrast into the deep system, subsequent fluoroscopic imaging of the infrainguinal deep venous system. A femoral injection may be necessary to study the central veins, with additional contrast injected as needed to image problem areas.

Filling defects, or the outlining of thrombus by contrast, define the level and extent of thrombus. Additionally, identification of collaterals, nonfilling of veins, and diversion of flow may indirectly *suggest* the presence of acute or chronic thrombus.

Descending venography is performed primarily to define the level of deep venous incompetence. The femoral vein is accessed percutaneously and a catheter placed in the external iliac vein. While the patient performs a sustained Valsalva maneuver, contrast material is hand injected while serial images are obtained. Venography is difficult to reproduce, has a high rate of interobserver disagreement, and is nondiagnostic in 4-10% of exams performed.[4] As with any invasive exam, venography carries certain risks, including exposure to radiation and complications directly related to contrast injection such as pain and/or phlebitis at the injection site, allergic reaction or anaphylaxis, venous thrombosis, and nephrotoxicity. Flushing of the veins post procedure with 50 cc of 0.45 normal saline, early ambulation, and adequate oral intake markedly decrease the incidence of side effects related to contrast.

There is mounting evidence that thrombolytic therapy for acute DVT achieves a significantly better short- and long-term clinical outcome than conventional heparin/anticoagulation therapy.[5] Theiss et al. showed that patients who presented three days, one to two weeks, and three to four weeks after the initial presentation of symptoms had complete or partial resolution of their DVT in 95%, 82%, and 69% of cases, respectively.[6] Therefore, thrombus delineation and staging becomes paramount. Acute venous thrombosis usually presents as a central filling defect within a dilated vessel, while a more chronic or subacute thrombosis will generally show a vessel with a diminutive caliber and variable collateralization. Herein lies the main difference between CTV and MRV as far as thrombus is concerned. CTV does not have the ability to define the age of a thrombus. An acute thrombus can even be seen on a noncontrast study as a hyperdense mass within the lumen of the vessel or in a contrast study as a filling defect with indirect signs such as soft-tissue enhancement.[7] On the other hand, MRV has been used to accurately stage a thrombus in a porcine model. This is based on changes in oxygenation states of the hemoglobin over time, changes in intracellular and matrix content of proteins, and the hydration of cellular components.[8]

Duplex ultrasound remains the gold standard for detection of DVT. This exam is noninvasive, relatively inexpensive when compared to other forms of imaging, painless, and uses no radiation; it is highly reproducible and has a low degree of interobserver variability.[9-11] It does, however, have some limitations. The studies can be time consuming and are highly technician dependent. Additionally, central veins including the iliacs can be challenging to define, and additional imaging exams are necessary to detect PE. Both CTV and MRV solve many of these issues in that they can visualize the

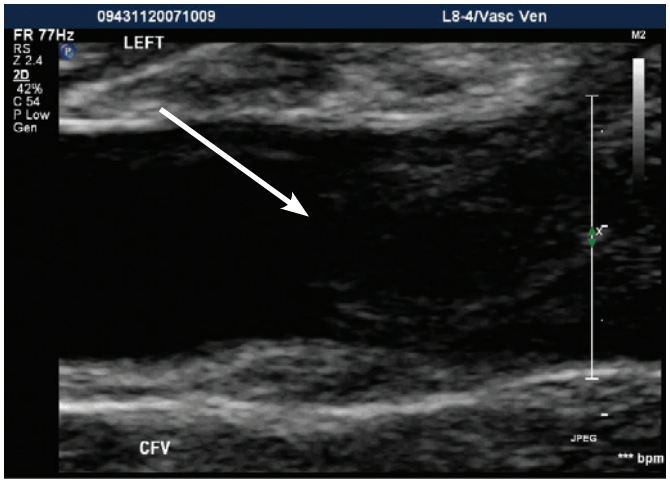

Figure 2. Duplex image of acute common femoral vein thrombosis in patient with pulmonary embolism. Arrow depicts leading edge of thrombus.

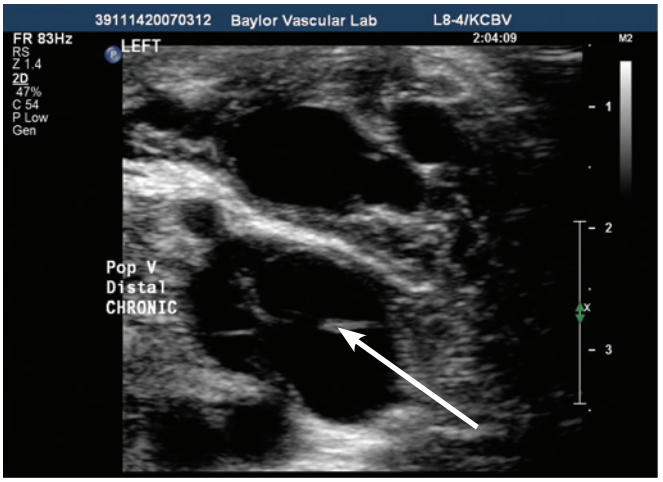

Figure 3. Duplex image of chronic partial common femoral vein thrombosis (arrow).

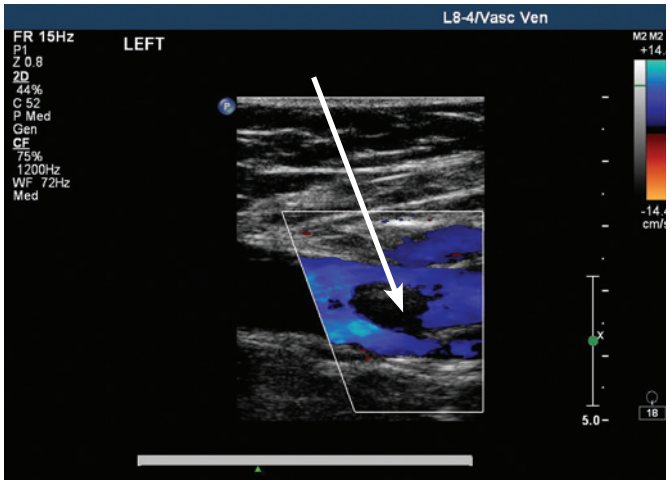

Figure 4. Duplex image of acute common femoral vein thrombosis outline by color Doppler. Arrow points to thrombus.

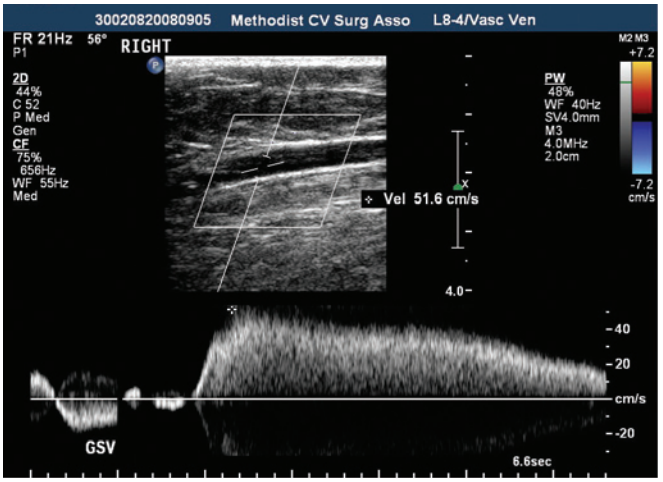

Figure 5. Doppler spectral waveform demonstrates incompetence, measuring duration of reflux. Flow above the baseline is abnormal.

peripheral and central veins and the pulmonary vasculature, potentially delineate the cause for DVT (i.e., May-Thurner, malignancy, etc…), and display the extent of collateralization. Duplex ultrasound has been studied extensively and is known to have a high specificity and sensitivity. In order for MRV and CTV to replace DUS, they must offer more than just concurrent imaging of the pulmonary vasculature; they must match or exceed the accuracy of ultrasound.

The sensitivity and specificity of DUS in the diagnosis of extremity DVT is >95%; however, calf sonography is not routinely done in all vascular labs. In any case, the significance and the need to treat these thrombi are controversial. Normal veins have thin walls, are echo-free, and collapse completely with light probe pressure. Acutely thrombosed veins appear dilated, have low-level echoes noted in the lumen, and do not compress or are partially compressible with pressure of the ultrasound probe (Figure 2). Chronically thrombosed veins may be small or of normal caliber and have brightly echogenic material in the lumens (Figure 3). The entire lengths of both the deep and superficial veins of the extremity are studied in a methodical manner.

Color Doppler is then applied, with the vein in a long axis approach. Pulsed-wave Doppler information from the interrogated veins is used to determine direction and velocity of flow, creating a color map of the veins. Abnormal areas of color flow aid in sample placement of the Doppler cursor for assessment of spectral waveforms increasing the sensitivity of the exam.[1] Proximal or distal augmentation maneuvers while observing velocity and spectral waveform changes are performed. Color Doppler and spectral waveforms are used to delineate venous anatomy, assess venous flow dynamics, identify thrombus location and extent (Figure 4), assess for valvular incompetence (Figure 5), and give

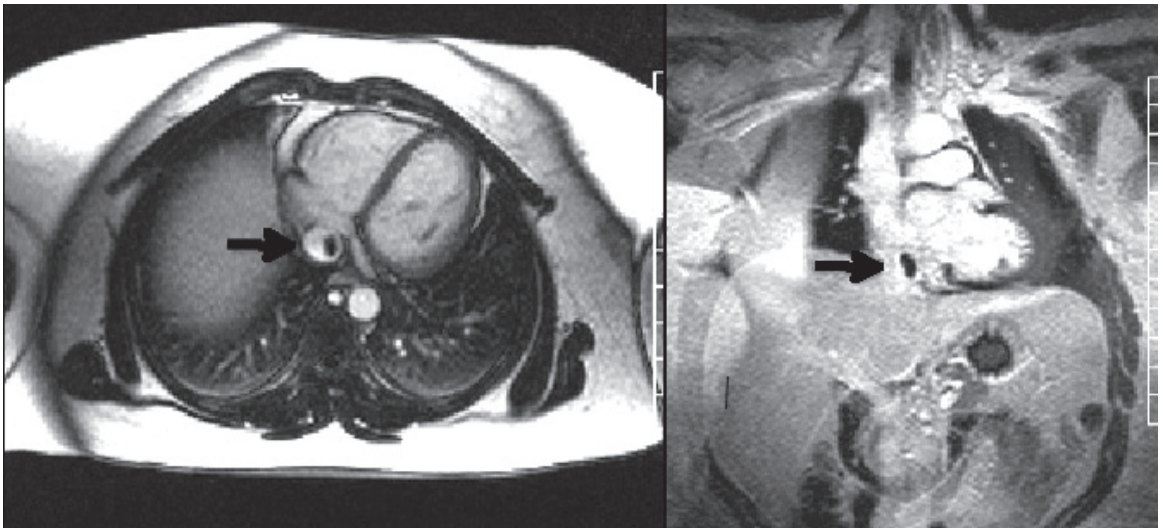

Figure 6. Delayed magnetic resonance venography for detection of thrombus

indirect information about the patency of more proximal veins.

CTV has been studied quite thoroughly in the Prospective Investigation of Pulmonary Embolism Diagnosis (PIOPED II) Study. Actually, it was found that the sensitivity and specificity of CTV and sonography was equivalent in diagnosing or excluding DVT.[13] Furthermore, it was found that one could perform a CTV as discontinuous images (every 15 mm) as opposed to continuous (7.5 mm) while still maintaining a high degree of reliability. The kappa statistics show a high level of agreement ($\kappa = 0.75$) between the two techniques while also reducing pelvic radiation by 75%.14 Based on these results from the PIOPED II trial, the recommendations for low, moderate, and high probability uses combined CTA/CTV as the initial radiographic study. In a moderate probability clinical assessment, the positive predictive value (PPV) was 92% and 90% for CTA and CTV respectively. For a high probability clinical setting, the positive predictive value was 96% for CTA and CTV.[15]

Should all patients suspected to have a VTE have a CTA/CTV? It is clear that patients who clinically are less likely to have a DVT have a lower PPV for CTV (57% for the low probability group in PIOPED II), and therefore one should not resort to ordering a CTA/CTV on all patients with suspected PE/DVT. The proportion of patients with a VTE who are diagnosed on the basis of a positive CTV is 14% on average, but remaining cost-effective should mandate being more restrictive.[16] When comparing MRV to contrast-enhanced venography, Laissy et al. found that MRV was 100% sensitive and specific. The differences in sensitivity and specificity as compared to duplex ultrasound were nonsignificant, showing noninferiority of MRV.[17]

How then does MR compare to CT for not only diagnosing DVT but also for the combined evaluation of a PE and DVT? In a meta-analysis, it was found that the pooled estimate of specificity and sensitivity were 94.8% and 91.5%, respectively. Furthermore, it was found that the sensitivity and specificity were equivalent for DUS and MRV.[18] Although the numbers are promising, they must be interpreted with caution as multiple MR sequences were used and the data may therefore not be directly comparable. Nevertheless, investigators are obtaining good results with both nonenhanced and contrast-enhanced MRV for DVT detection, comparable to CTV.[19, 20] MRV has also been proposed as a "problem-solving" modality, particularly for imaging the pelvic veins. The true incidence of pelvic thromboses is underrated with ultrasound, and MRV has been able to show this.[12] MRV is also valuable in viewing the central veins.

As far as PE is concerned, a study examined 207 patients with combined studies for DVT/PE. Three thoracic sequences were evaluated (true-FISP, pulmonary perfusion, and thoracic angiography), and pulmonary perfusion was found to be the most robust with a sensitivity of 93-100% and specificity of 91-94%.[21] MR-venography detected DVT in 13 patients with a negative PE study, or 17.1% more DVTs, as compared to ultrasound. CT also showed similar diagnostic accuracy ($\kappa = 0.86$).[21-24] The conclusion must therefore be that MRA/MRV is equivalent to CTA/CTV. The issue for MR remains a question of sequences, and we would recommend a combination of time of flight (TOF) sequence and a T1 post-contrast sequence in acute settings. We have used a TR-600 sequence with significant delays of up to 40 minutes, at which point the only intravas-

cular structure that would be black on imaging would be thrombus. With this technique we have been able to differentiate bland thrombus from tumor thrombus (Figure 6).

Varicose Veins (Vv) and Venous Insufficiency (Vi)

Varicose veins (VV) are extremely common and estimated to be present in some form in approximately 30-60% of adults in the world. The incidence is 13.5 per 1,000 person years.[25, 26] The development of less invasive treatment modalities has revived the interest of both the public and medical community. Currently, the most common diagnostic tool used for evaluation of venous insufficiency is DUS, which is readily available and provides reliable information on both the anatomy and hemodynamics associated with venous disease (Figure 7). As discussed previously, ultrasound remains technician dependent and in some instances is unable to provide the root cause of the varicosities or ulcer (i.e., secondary reflux, distribution of varicosity and perforating veins), information needed to successfully manage venous disease.[27] Although the exam for venous insufficiency is time consuming and may take up to 1½ hours to perform, the exam is noninvasive and inexpensive when compared to CTV and MRV and carries no risk. Other factors that may limit the venous DUS may include the presence of fresh incisions, casts or occlusive dressings, edema and large limbs or abdomen, or a patient unable to lie in a supine position for an extended time. Large fields-of-view provided by CTV and MRV allow for more detailed preoperative evaluation of the limb with venous insufficiency, an additional limitation of DUS where only very narrow fields-of-view are provided.

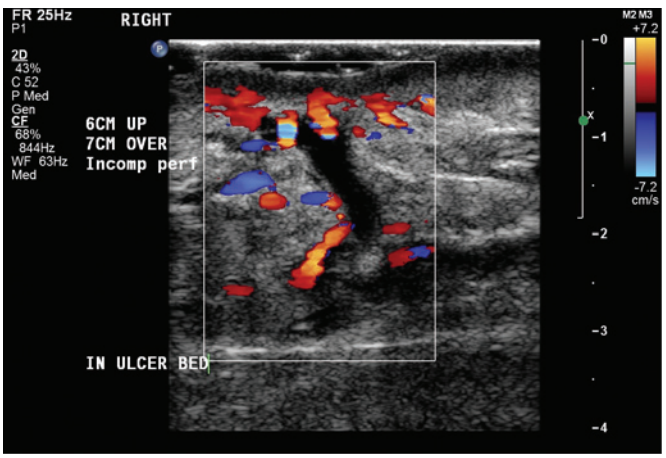

Figure 7. Duplex image of incompetent perforating vein (arrow) in highly vascular ulcer bed.

Lee et al. showed, in 100 consecutive patients, that CTV performed with the patient in the supine position correlated well with ultrasound findings ($\kappa = 0.72$). On CTV, the mean diameter of greater saphenous veins found insufficient with duplex sonography was 7.0 mm and the mean diameter of GSVs found competent was 4.9 mm ($p < 0.001$). The sensitivity and specificity of CTV to predict greater saphenous vein insufficiency was 98.2% and 83.3%, respectively.[27] All patients had indirect CTV with instillation of contrast via an antecubital vein and a scan delay of three minutes. Uhl et al. found CTV particularly useful in revealing the reason for varicose vein recurrence.[28]

As already discussed, the successful management of VV is dictated by thorough preoperative evaluation revealing all sources of reflux. Muller et al. evaluated the use of direct contrast-enhanced MRV in managing recurrent lower extremity VVs. Contrast was injected via a pedal arch vein, and veins were considered significant if they were measured to be greater than 3 mm. MRV depicted significantly more incompetent veins, which affected management in 77% of legs evaluated. Surgical management of these incompetent veins confirmed MRV findings, and even more importantly, two independent readers detected the same incompetent veins in all legs examined ($\kappa = 1.00$).[29] Likewise, Ruehm et al. found direct MRV of VVs comparable to conventional contrast-enhanced venography, with a sensitivity and specificity of 94% and 96%, respectively.[30] Unenhanced techniques are also available for imaging of lower extremity veins. Edelman et al. used signal targeting alternative radiofrequency and flow-independent relaxation enhancement (STARFIRE) to demonstrate the feasibility of MRV in evaluating lower extremity veins. The optimal inversion times (TI) were 900 and 1,500 msec, because as the signal intensity of blood vessels increases as the TI is shortened, so does the fat signal. This also means that fluid or edema will appear white, but this can easily be edited out.[31] The advantage of this technique is again its large field-of-view, while its major limitation is the lack of hemodynamic feedback.

Dynamic Imaging

Variations in IVC wall motion and caliber have been attributed to changes in blood flow through the low-pressure caval system in response to changes in intrathoracic pressures. During inspiration, negative pressure in the chest draws blood from the IVC, causing the IVC to diminish in size. The contrary is seen during expiration, as positive intrathoracic pressure diminishes blood flow into the heart, allowing the IVC to fill and expand. A Valsalva maneuver — for example, during

defecation, heavy lifting, and coughing — is a sustained expiratory effort against a closed glottis resulting in markedly increased intrathoracic pressures. This maneuver also increases the size of the IVC as flow into the chest is impeded, much like vena cava engorgement in right-sided heart failure. Understanding the dynamic nature of the venous system is imperative in the ability to best utilize the three modalities discussed in this paper. Using computational fluid dynamics, we have been able to define this movement, as depicted in Figure 2. Knowledge of venous system hemodynamics will allow integration of the motion as the fourth dimension to better understand and interpret a patient's physiology. This will potentially promote more targeted and precise therapies, thereby improving patient outcomes.

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