Outpatient Management of Deep Venous Thrombosis

Urgent message: Urgent care providers are on the frontline in diagnosis of DVT. Outpatient management is a consideration for carefully selected patients.

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Deep venous thrombosis (DVT) is formation of a clot in the deep venous system, usually in a lower extremity. Half of untreated patients with DVT will go on to develop the fatal complication pulmonary embolism (PE). Approximately 300,000 to 600,000 Americans die each year due to venous thromboembolism (VTE).[1]

Urgent care providers are typically the frontline for patients with acute leg pain, swelling and discoloration. A systematic approach to ruling out DVT will help get patients the appropriate care. Many urgent care centers do not have ready access to compression ultrasound, which is the gold-standard test to rule out DVT. Studies have shown that with use of a D-Dimer assay and risk stratification with the Wells criteria, providers can distinguish which patients need further study and which can be safely ruled out. These diagnostic criteria are proven to be superior to clinical judgment alone. With use of Wells Criteria and D- Dimer testing; only 1% of DVTs are missed. With use of clinical judgment alone, 5% of DVTs are missed.[2]

This article discusses how to use the Wells criteria as a clinical predictor for DVT and how the point-of-care D-dimer test contributes to decision-making. We will also discuss criteria for inpatient versus outpatient management of DVT, available treatment options, duration of therapy, and how this all relates to an urgent care setting.

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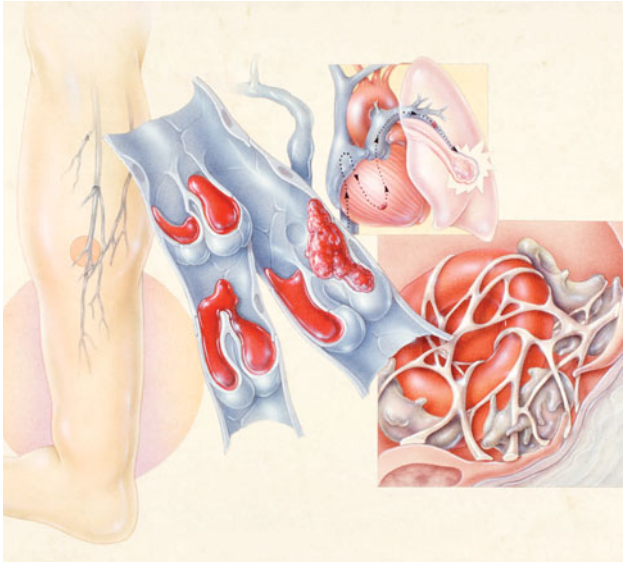

Risk Factors for DVT and Patient History

Risk factors for DVT can be remembered by recalling Virchow's Triad: venous stasis, endothelial damage, and hypercoagulability.

In addition, one-third of patients who suffer from a DVT will have recurrence within 10 years.[1]

A history of immobilization, exposure to long-haul flights, and prolonged hospitalization all are risk factors for venous stasis. Hospitalized patients are now given compression stockings or low-molecular-weight heparin injections to combat venous stasis thus preventing DVT in the inpatient setting.

Recent surgery, trauma, or presence of an infectious disease are examples of endothelial damage that can lead to DVT.

Pro-thrombotic states such as cancer, stroke, pregnancy, hormone therapy, obesity, and inheritable thrombophilias can also lead to DVT. Hormone therapy includes oral contraceptives, hormone replacement therapy, and appetite stimulants such as megace/megestrol. Inherited thrombotic states include protein C and S deficiency, anti-thrombin 3 deficiency, antiphospholipid antibody, hyperhomocysteinemia, factor V Leiden, and others.

Who should get a work up for thrombophilia and when? It is not cost-effective to test everyone with a DVT for a hypercoaguable state. Individuals with an unprovoked DVT prior to age 50, those with recurrent DVT, and patients with a family history of thrombotic states all warrant testing. Testing should occur prior to the start of therapy or 2 weeks after stopping therapy because treatment can interfere with the accuracy of test results.[3]

Differential Diagnosis

What are the differentiating features of DVT? How do you distinguish DVT from other diagnoses such as cellulitis, superficial thrombophlebitis, venous insufficiency, lymphedema, muscle tears, hematoma, and ruptured Baker's cyst? These differentials can often mimic DVT because they present with unilateral calf swelling and tenderness. Key elements in the history and physical can lead to the correct diagnosis. We will first discuss presentations of unilateral leg swelling in the acute setting.

Cellulitis of the lower extremity can be unilateral and present with swelling. The features that differentiate cellulitis from DVT are the infectious process, which often is associated with a precipitating factor such as a break in the skin. Because cellulitis is infectious, patients with it will also have constitutional

Table 1. Wells Prediction Rule for Diagnosing DVT

Clinical characteristic	*Score*
Active cancer (treatment within last 6 months or palliative)	1
Calf swelling where affected calf circumference measures >3 cm more than the other calf (measured 10 cm below tibial tuberosity)	1
Collateral superficial veins (nonvaricose)	1
Pitting edema (confined to symptomatic leg)	1
Swelling of entire leg: 1 point	
Localized pain along distribution of deep venous system	1
Paralysis, paresis, or recent cast immobilization of lower extremities	1
Recently bedridden for >3 days or major surgery requiring regional or general anesthetic in past 4 weeks	1
Previous history of DVT or PE: 1 point	
Alternative diagnosis at least as probable	-2
Risk score interpretation (probability of DVT): 3 points: high risk (75%); 1 to 2 points: moderate risk (17%); <1 point: low risk (3%).	

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symptoms such as fever and lymphadenopathy.

Thrombophlebitis or superficial venous thrombosis (SVT) is a non-infectious process that is due to inflammation and/or clotting of superficial veins. The patient history will often include varicose veins, which is the most common predisposing factor to SVT. The differentiating feature on physical exam is the presence of a painful, warm, palpable superficial vein. For diagnostics, an ultrasound is warranted to rule out concomitant DVT. The mainstay of therapy for SVT is nonsteroidal anti-inflammatory drugs (NSAIDs) and compression stockings. If the location of the clot is near the saphenous-femoral junction, anticoagulation should be given for 1 month because of the high risk of progression to DVT.

Medication side effects can also be a cause of lower-extremity edema. Common culprits are calcium channel blockers such as amlodipine, vasodilators, and drugs that trigger salt retention.

A ruptured popliteal cyst or Baker's cyst can present as unilateral leg swelling and discomfort. On exam, patients with the condition will present with fullness behind the knee due to synovial fluid accumulation in the bursa. Their history will often include rheumatologic disorder such as arthritis. The popliteal bursa can rupture, causing synovial fluid leakage and calf swelling. The treatment for this is often supportive care with close follow up to monitor for resolution. In extreme cases, the fluid can compress the deep veins of the calf and lead to DVT from venous stasis.

Muscle rupture and or hematoma can also cause unilateral swelling and pain. The patient will often give a history of trauma or new-onset strenuous exercise and subsequent development of a painful calf. The treatment here is largely supportive care.

Conditions that can cause edema in a chronic setting are venous insufficiency, lymphedema, and exposure to certain medications.

Venous insufficiency is a chronic cause of unilateral leg edema. The etiology is due to insufficient valves that cannot effectively pump blood back to the heart. Venous blood accumulates in the lower extremity, causing swelling. These patients will often have a differentiating feature on exam of hyperpigmentation and/or ulceration to the skin that is not seen with DVT. Another key feature is time. Venous insufficiency is a chronic condition that occurs over several months, whereas patients with DVT will present in a more acute setting.

Lymphedema, another chronic cause of leg edema, is accumulation of lymph fluid in the interstitial space due to obstruction of lymphatic flow. A key differentiating factor is timing. The development of swelling is slow in onset whereas DVT is usually rapid onset. Patients with lymphedema can present with a recent surgical history of lymph node dissection and subsequent swelling of an adjacent limb. The skin will also appear thickened and fibrous over time unlike an acute DVT presentation.

Physical Exam

Certain physical exam findings will lead an urgent care provider to include DVT in the differential diagnosis. It should be noted, however, that physical findings alone cannot be used to rule out a DVT.

Begin your exam by comparing the lower extremities, looking for a difference in calf circumference, swelling, erythema, or mottling of the skin. The affected extremity should be examined for a palpable chord and/or calf tenderness. Pain with dorsiflexion of the foot is a clinical sign of DVT (Homan's sign.) A thorough vascular exam should also be done.

Diagnostics

In the outpatient setting, DVT can be ruled out with a

combination of two tools: Wells criteria and a D-dimer blood test. Patients can be risk-stratified with the Wells criteria into a high- or low-risk category for DVT (**Table 1**). A negative D-dimer test in conjunction with a low-risk score on Wells criteria can rule out DVT.[4]

The Wells criterion, which generates a possible score of -2 to 9, is a tool used to predict DVT. A score of 2 or greater places the patient at high risk of DVT and warrants imaging with venography. A low score of less than 2 puts the patient in a low-risk category and should be used in conjunction with a negative D-dimer test to rule out DVT.

What is the D-dimer and how good a test is it? D-dimer is a measure of the degradation of fibrin. In point-of-care testing, it has good negative predictive value, and a high sensitivity (91%-99%) but an average specificity of 60% for DVT.[2] Because the assay for D- dimer is not specific, a false-positive result is possible in association with any fibrinolytic process, such as cancer, surgery, disseminated intravascular coagulation (DIC) or trauma. A false-negative, on the other hand, is possible in a patient taking anticoagulation therapy. A D-dimer assay also is less accurate 1 week after the start of symptoms.[5]

Five different D-dimer point-of-care tests are commercially available: Vidas, pathfast, cardiac, triage, and the simple clearview. The first four are quantitative tests; clearview is the only qualitative test. A head-to-head comparison of the D-dimer studies for both accuracy and user-friendlines concluded that all five tests have high sensitivity or a high negative predictive value of 98%. However the most user-friendly tests are the triage and clearview D-dimer studies. Both require little calibration and therefore, are associated with fewer operator errors.[2,6]

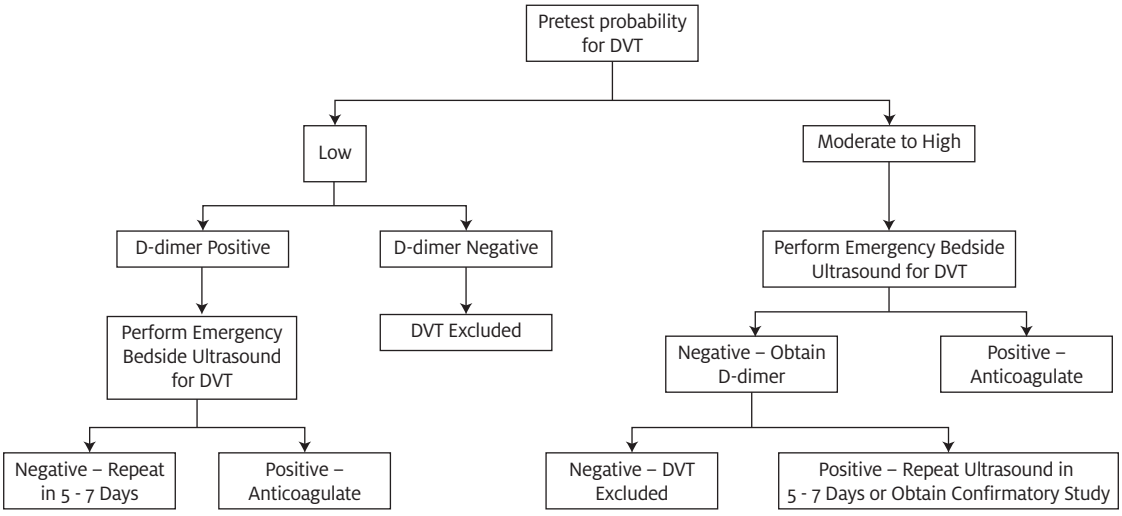
How does point-of-care testing for D-dimer compare with traditional central lab testing? A bioequivalence study was done in the emergency room setting to answer that very question. The study compared the Vidas point-of-care test with the traditional central lab D-dimer and found that point-of-care testing had a faster turnaround time by about 101 minutes. However, the Vidas test only predicted 83% of positive results from the central lab. The point-of-care test, therefore, while quicker is less accurate.[7] The study was limited in that it did not compare the other four available point-of-care tests for D-dimer. The gold-standard central lab test is a standard ELISA assay that has a sensitivity of 85% to 89%. Both the clearview and cardiac D-dimer studies have shown equivalent or greater sensitivity.

Does point-of-care testing have a place in the outpatient setting? It does in patients who fall into the low-risk category using the Wells criteria. A low-risk patient with a negative D-dimer point-of-care test can be safely ruled out and sent home.

Medical Decision-Making

If a DVT is suspected, the first step is calculation of the pretest probability with the Wells criteria. If the score is low or (less than 2), then a D-dimer should be checked. If the D-dimer is negative, DVT can be safely ruled out. If the D-dimer is positive, an ultrasound should be performed.

Figure 1. DVT Clinical Algorithm



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If the Wells score is moderate/high, the first step is an ultrasound. If the ultrasound is positive, proceed with anticoagulation. If the ultrasound is negative, a D-dimer should be obtained to exclude DVT. If the D-dimer is positive and the Wells score is high, ultrasound should be repeated in 1 week to confirm accuracy of the study. The diagram in **Figure 1** very simply outlines the care path based on a patient's risk in conjunction with D-dimer testing.[8,9]

Treatment

Once a diagnosis of DVT has been made, what are the treatment options, what are the goals of therapy, and what is the duration of therapy recommended? Which patients are candidates for outpatient treatment and when should a patient be admitted for therapy?

The goal of treatment is to prevent DVT from developing into a fatal PE. Two distinct options exist for outpatient therapy: Low-molecular-weight heparin (LMWH) in combination with oral warfarin or oral rivaroxaban. Oral warfarin should be started at the same time as intravenous (IV) unfractionated heparin or subcutaneous LMWH. When an INR of 2 to 3 is achieved, heparin can be stopped and oral warfarin continued. The recommended starting dose of warfarin is 10 mg. LMWH is dosed by weight: 1 mg/kg subcutaneously (SQ) twice daily or 1.5 mg/kg once a day. Heparin should also be renally dosed. This treatment pathway would require lengthy patient education, including instructions on how to administer enoxaparin and dietary restrictions. Prior to discharge patients will also need primary care follow up for international normalized ratio (INR) monitoring to ensure therapeutic dosing. The enoxaparin/warfarin combination is a challenging treatment model in the urgent care setting for these reasons. A lot of resources and time are needed to ensure patient safety.

Rivaroxaban is a newer medication for anticoagulation that works by inhibiting coagulation factor Xa. The advantage of this medication is that it can be taken once a day orally. There is no need to bridge therapy with IV or SQ medication. Routine lab testing for INR is also unnecessary. The Einstein study published in *The New England Journal of Medicine* found that treatment of acute DVT and long-term treatment of DVT is safe and as effective as the traditional therapy with LMWH and oral warfarin. The study also found that there is an acceptable, low risk of bleeding with oral rivaroxaban and low risk of recurrence when treatment is completed.[10]

The disadvantage is there is no way to reverse the effects of the medication in the event of bleeding. In addition, there is no blood test to check for patient compliance. The burden of effective therapy is transferred from doctor to patient. Rivaroxaban cannot be given to patients with a creatinine clearance less than 30. Prac-

Table 2. Duration of Treatment

NO treatment Distal LE DVT, asymptomatic and IF doesn't extend when followed with serial imaging. (Treat if extends.)
3 months Distal LE DVT, symptomatic (regardless of cause), or extending asymptomatic Surgery or risk factor- associated proximal LE DVT (regardless of symptoms) Unprovoked proximal LE DVT if high bleed risk Recurrent, unprovoked LE DVT or PE (high risk)
Extended/Lifetime Unprovoked proximal LE DVT (if low or moderate bleed risk) Cancer-associated DVT or PE (LMWH preferred over warfarin)

DVT = deep venous thrombosis; LE = lower extremity; LMWH = low-molecular-weight heparin; PE = pulmonary embolism

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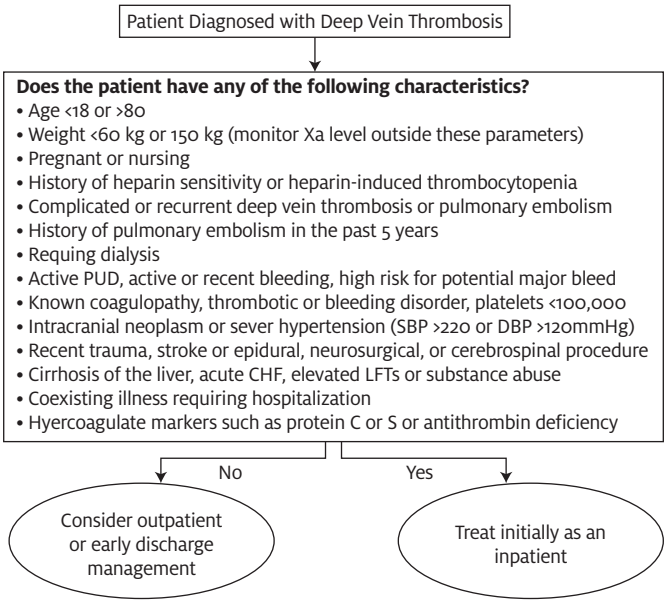
Figure 2. Guidelines for the Outpatient or 'Early Discharge' Management of DVT



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titioners should calculate the creatinine clearance with the Cockcroft –Gault formula to ensure that a patient is a good candidate for the drug.

Oral rivaroxaban is an excellent option for treatment of acute DVT in the urgent care setting for a few reasons. The need for extensive patient education is eliminated because drug administration is simply swallowing a pill. Furthermore, follow up does not need to be arranged prior to discharge because the drug does not need to be titrated nor an INR followed. The medication has no dietary restrictions. An urgent care provider would need a confirmatory ultrasound test to confirm a diagnosis of DVT and then treatment could be started in the urgent care setting.

The length of anticoagulation therapy is dependent upon the individual patient and is similar for treatment with either model enoxaparin or rivaroxaban. Treatment duration is at least 6 weeks to 3 months. A duration of 3 months is appropriate for the patient with a first DVT that is provoked. Treatment for 6 months is appropriate for an unprovoked first DVT. For recurrent DVT or a known prothrombotic condition, the duration of treatment is 12 months. **Table 2** illustrates factors that impact treatment duration.

What are the indications for inpatient versus outpatient management of DVT? How can urgent care providers better facilitate patient transfer of care when needed? **Figure 2** provides guidelines to help determine proper patient disposition.

Outpatient management is considered safe and effective therapy for DVT in appropriately selected individuals. Patients should be screened using the previously described inpatient criteria. They must also have a solid understanding of their condition and appropriate follow up. A supportive family and/or friends to help facilitate compliance, a working phone to call for help in the event of bleeding, and a way to return to the hospital in the event of an emergency are additional important

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factors, as is adequate pain control while at home. If these conditions are met, a patient can be considered a good candidate for home treatment with either enoxaparin or oral rivaroxaban.[3]

Conclusion

Many patients present to urgent care centers with symptoms of acute onset unilateral leg swelling. DVT is frequently in the differential diagnosis. Because of the high morbidity and mortality associated with progression of DVT to PE, a systematic approach must be taken to safely rule out VTE in the outpatient setting. The initial step with the Wells criteria helps to establish a patient's risk. High- or moderate-risk patients should be referred for Doppler ultrasound testing. Low-risk patients can have the D-dimer assay checked, and if the results are negative, DVT can be safely ruled out. Once the diagnosis is made, treatment decisions, including options for outpatient therapy, depend on individual patient characteristics. For the right patient, outpatient treatment can be considered and can be effectively managed in the urgent care setting. ■

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