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Urgent Care Diagnosis and Management of DVT

Urgent message: Screening patients with suspected deep vein thrombosis using the Wells' criteria is an efficient tool that would be even more impactful with access to point-of-care, high-sensitivity D-dimer testing in the urgent care setting.

JOHN DESMARAIS, MD and SAMIDHA DUTTA, DO

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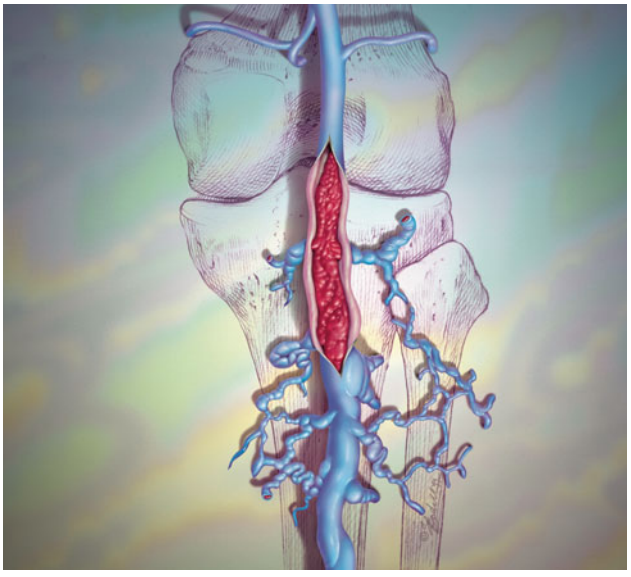
Case Presentation

A 37-year-old woman presents with 3-day history of right leg swelling and pain. Symptoms began with no history of trauma. She denies prior episodes. Her symptoms have persisted despite using ibuprofen, warm compresses, and massage to the area. She has pain with ambulation. Her past medical history includes hypertension for which she takes only lisinopril. She denies tobacco or illicit drug use, and drinks alcohol only on holidays. She lives an active lifestyle.

Her right calf is warm and erythematous. Palpation of the posterior calf elicits pain. There is nonpitting edema. The right calf is 1 cm greater in diameter than the left. The remainder of her exam is unremarkable. Vitals are normal. She seems uncomfortable when trying to ambulate on the leg but is in no acute distress.



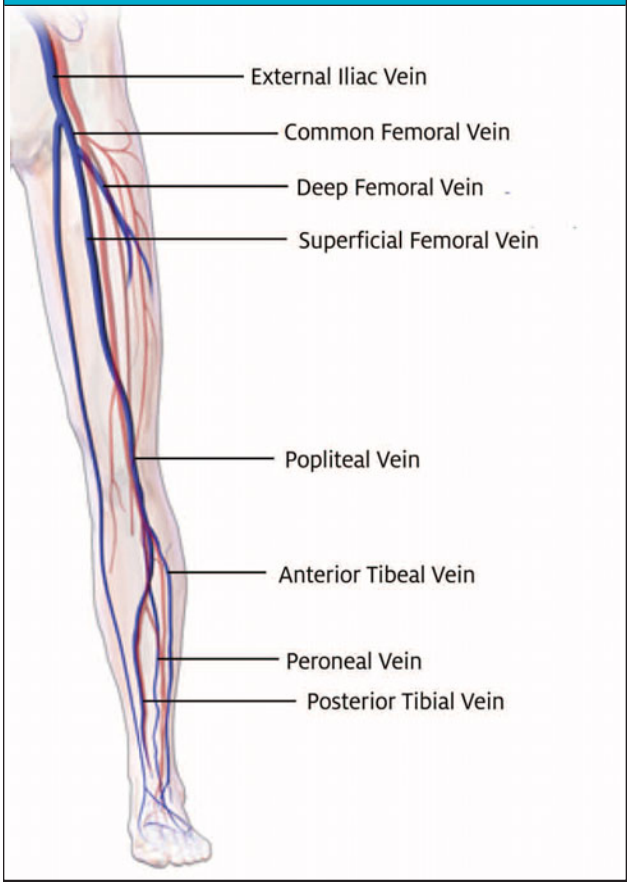
Introduction

A deep vein thrombosis (DVT) can occur in any of the deep veins (**Figure 1**). According to the American Heart Association, it is the third most common vascular diagnosis following myocardial infarction and stroke and affects roughly 300,000 to 600,000 Americans annually.[1] DVTs most commonly involve clot formation in the large veins of the lower extremity and can be either proximal or distal to the knee. A pulmonary embolism (PE) occurs when the thrombus dislodges and travels proximally through the venous system into the pulmonary vasculature. The risk of DVT increases by 60% in individuals over 70 years of age. Approximately half the individuals with untreated proximal DVT develop symptomatic PE within a period of 3 months and 25% of these symptomatic cases result in sudden death.[2]

Though often not readily available in urgent care or primary care, venous ultrasound is the test of choice for DVT. Thus, history, physical exam, and risk stratification are essential in determining when and how rapidly testing should occur. An important risk stratifying tool is the Wells' score for DVT (**Table 1**). Distinguishing between "provoked" and "unprovoked" and "first-time" vs "recurrent" DVT has important implications for formulating management.

Author affiliations: John DesMarais, MD is program director, Adena Family Medicine Residency. **Samidha Dutta, DO, PGY-3** is a third-year resident in the Adena Family Medicine Residency. The authors have no relevant financial relationships with any commercial interests.

Figure 1: Deep veins of the lower extremity



Risk Factors

The highest risk in females occurs before 50 years of age. In males, DVT occurs more commonly over 65 years of age.[3] Other nonmodifiable risk factors include the presence of inherited thrombophilias such as Factor V Leiden mutation, prothrombin gene polymorphism, protein C and S deficiency, non-O blood groups, and methylenetetrahydrofolate reductase (MTHFR) gene polymorphism, with the risk greatest in those who are homozygous for these conditions.[2,3] The most potent of these genetic risk factors are protein C and S deficiencies, which are present in approximately 15% of patients under the age of 45 who present with a DVT. Deficiency in either of these proteins can increase risk of DVT by 10-fold or more.[2]

Factor V Leiden mutation, the most prevalent of these genetic conditions, is associated with a lifetime incidence of DVT of about 6.3%.[3]

Thrombophilias should be suspected in patients with history of recurrent DVT or recurrent miscarriages. Family history of thrombophilias in first-degree relatives is also an important component of history-taking in patients with signs and symptoms of DVT.

Table 1. Wells' Criteria for DVT

Risk factors	Points
Active cancer	1
Bedridden recently >3 days or major surgery within 12 weeks	1
Calf swelling >3 cm compared to the other leg	1
Collateral (non-varicose) superficial veins present	1
Entire leg swollen	1
Localized tenderness along the deep venous system	1
Pitting edema, confined to symptomatic leg	1
Paralysis, paresis, or recent plaster immobilization of the lower extremity	1
Previously documented DVT	1
Alternative diagnosis to DVT as likely or more likely	- 2

Acquired and Persistent Factors

The risk of DVT events is several times higher in patients with congestive heart failure (CHF) under the age of 40 compared with those over age 80. Patients with CHF have increased venous stasis resulting from decreased cardiac output and patient immobility. Increasing severity of heart failure is directly correlated with an increased incidence of DVT.[2]

The overall risk of DVT in patients with advanced cancer increases by seven-fold when compared with the general population.[2] Certain cancers such as non-Hodgkin lymphoma, lung, ovarian, brain, pancreatic, and gastrointestinal have higher rates of associated DVT.[2] Chemotherapeutic agents such as 5-fluorouracil, tamoxifen, and cisplatin are all medications that influence factors such as hypercoagulability, endothelial injury, and/or blood flow which in turn also contributes to the increase risk of DVT in patients with cancer.[2]

Several other acquired risk factors include acute infection, chronic inflammatory diseases (eg, systemic lupus erythematosus, rheumatoid arthritis), chronic obstructive lung disease, chronic kidney disease, recent history of stroke (with an increased incidence of DVT by 15% in patients within the first 3 months post-stroke), recent major surgery (especially orthopedic surgeries), and trauma (eg, spinal cord injuries).[2,3]

DVT risk increases in a dose-dependent manner in response to estrogen levels, especially in patients on

Table 2. Anticoagulant Options

Direct factor Xa inhibitors			
Apixaban (Eliquis)	10 mg twice a day for 7 days then 5 mg twice a day	27% renal clearance Adjust dose if CrCL <15 mL/min	$300 to $500 per month Free 30-day coupon Bristol-Myer Squibb
Edoxaban (Savaysa)	>60 kg = 60 mg daily <60 kg = 30 mg daily after 5 to 10 days of parenteral bridging	50% renal clearance Avoid use if CrCl <15 or >95 mL/min	$350 per month No coupon or patient assistance program
Rivaroxaban (Xarelto)	15 mg twice a day for 21 days then 20 mg daily	66% renal clearance Avoid used if CrCl <30 mL/min	$350 to $600 per month No coupon Johnson and Johnson
Direct thrombin inhibitors			
Dabigatran (Pradaxa)	150 mg twice a day after 5 to 10 days of parenteral bridging	80% renal clearance	$300 to $500 per month Free 30-day coupon Boehringer-Ingelheim
Indirect factor Xa inhibitor			
Fondaparinux (Arixtra)	• <50 kg = 5 mg subcutaneous, daily • 50 to 100 kg = 7.5 mg subcutaneous daily • >100 kg = 10 mg subcutaneous daily • Concomitant treatment with warfarin should be initiated as soon as possible	100% renal clearance Avoid used if CrCl <30 mL/min	
Low molecular weight heparin			
Dalteparin (Fragmin)	• 100 units/kg subcutaneous q12hr • 200 units/kg subcutaneous daily	Primarily renally cleared	
Enoxaparin (Lovenox)	• 1 mg/kg subcutaneous q12hr • 1.5 mg/kg subcutaneous daily	Primarily renally cleared	

hormone-replacement therapy or taking combination oral contraceptives. Similarly, later stages of pregnancy and the puerperium period also increase the risk of DVT by a rate 1.4%.[3] This relation is also the understood mechanism for why premenopausal women, ie, those under the age of 50, have a higher incidence of DVTs.

Modifiable risk factors

Modifiable risk factors include obesity, increased waist circumference, and cigarette smoking. Obese individuals are twice as likely to develop DVT.[2] Patients with childhood obesity maintain an increased risk of DVT into adulthood even if BMI normalizes.[4] Metabolic disorders such as diabetes are also included in these lifestyle-related risk factors; other modifiable risk factors include immobilization, dehydration, and long-term steroid.[2,3]

Diagnosis

DVT can present with unilateral leg pain, swelling, and occasionally redness of the affected extremity. Often, the nonspecific nature of the complaint necessitates use of objective tests to confirm diagnosis.

D-dimer is among the most common screening tests for DVT and PE. D-dimer is a fibrin clot degradation product which is increased in patients with both acute and chronic thrombosis. Unfortunately, although very sensitive, its use is limited as a stand-alone test because its low specificity can result in frequent false positives. Many conditions, such as recent surgery, trauma, pregnancy, older age, and cancer can lead to D-dimer elevation.[4] Be-

Table 3. Anticoagulation Preferences in Different Clinical Scenarios[3]	
CKD Stage I-III (GFR >30)	Prefer DOACs
CKD Stage IV (GFR 15-29)	Prefer warfarin or half dose LMWH. Avoid DOACs
ESRD on dialysis	Prefer warfarin. Avoid DOACs and LMWH
Pregnancy	Prefer LMWH. Avoid DOACs and warfarin
Breastfeeding women	Prefer warfarin or LMWH. DOACs contraindicated
Non-GI tract cancer	Prefer LMWH or DOACs
GI tract cancer	Prefer LMWH or apixaban. Avoid rivaroxaban or edoxaban
Receiving chemotherapy	Prefer LMWH or DOACs (must assess chemotherapy-DOAC interaction)

cause of the low specificity, assessing pretest probability is often combined with D-dimer assay testing.

Interpretation of the Wells' Score

The Wells' DVT risk score is a validated tool widely used to help determine the pretest probability of DVT.[3] A score of 0 represents a 5% risk of DVT. A score of 1–2 represents a 17% risk and 3 or greater is associated with a 17% to 53% prevalence risk. Patients with the lowest Wells' score (-2) have up to a 5% risk of thrombus, underscoring that DVT cannot be 100% excluded using this alone.[3] Current recommendations favor a combined approach toward diagnosis: Patients with a score of ≤1 on the Wells' criteria have a low risk of DVT, so this should prompt a D-dimer test which, if negative, can reliably exclude the diagnosis. If the D-dimer is positive, a confirmatory diagnostic imaging test should follow. Patients with a high-risk Wells' score of ≥2 do not need a D-dimer but may proceed immediately to a diagnostic imaging test to confirm the diagnosis.[7]

D-dimer levels increase with age, leading to even lower specificity for DVT in older patients. An age-adjusted D-dimer threshold, defined as the patient's age multiplied by 10 ng/mL, has been suggested for patients older than 50 years.[4] This age-adjusted strategy improved specificity by about 9.5% from 45.2% to 54.7% and reduced false positives to a more acceptable level.[3,5]

In outpatient settings, the preferential diagnostic imaging choice should be venous compression ultrasound. Alternative imaging modalities like venography, CT, and MR venography can be utilized; however, this is a less desirable approach due to high cost, exposure to ionizing radiation, reaction to contrast media, or their invasive nature.

Differential Diagnosis

- Distal DVT – The ultrasound may demonstrate a distal DVT in one of the calf veins. Anticoagulation is controversial in these settings unless the patient has risk factors for extension (eg, an unprovoked DVT or previous venous thromboembolism) or develops extension on serial ultrasound exam, which should be done 2 to 3 weeks after the initial diagnostic investigation to exclude propagation of the clot.
- Severe calf muscle pull/trauma – History usually involves an injury and signs of bleeding on the ultrasound or hematoma formation or bruising at the ankle.
- Superficial thrombophlebitis – This classically presents as tender hard or red-appearing swollen superficial veins. Superficial thrombophlebitis may be associated with DVT and should be further evaluated with venous ultrasound.[3]
- Cellulitis – Cellulitis, like DVT, causes warmth, swelling, and redness of an affected extremity. Furthermore, the two conditions can co-exist and, therefore, ultrasound may be necessary in such presentations.
- Lymphedema – This is a cause of chronic edema. Since there are no distinguishing factors between lymphedema and edema associated with DVT, ultrasound is generally appropriate when there is acute increase in swelling or pain.
- Popliteal (Baker's) cyst – This is often distinguished from DVT by its presentation as posterior knee pain with knee stiffness and a swollen mass behind the knee. Ultrasound is still often performed nonurgently to confirm the presence of a full or partially drained Baker's cyst.
- Interstitial edema – Lower extremity edema is commonly found in patients with heart failure, liver disease, or can be associated with medications like dihydropyridine calcium channel blockers (amongst others). The edema in these cases is usually bilateral but can be asymmetric if accompanied by underlying venous pathology. Signs of inflammation are usually not present, and if the Wells' score is low risk and the D-dimer is negative then no further investigations need to be performed.[3]

Treatment

Anticoagulation is the mainstay for management of DVTs with the goal of preventing progression, recurrence, and providing acute relief of symptoms. Man-

agement of DVTs can be categorized into an acute phase and a chronic phase. The acute phase typically includes the first 3 to 6 months after onset. Most instances of DVT can be managed on an outpatient basis except in severe cases such as proximal clots (eg, common femoral and/or iliac veins), phlegmasia/limb ischemia, significant comorbidities such as end stage renal disease, and high bleeding risk.[6]

Among the options for anticoagulation are vitamin K antagonists such as warfarin, direct oral anticoagulants (DOAC), and low-molecular-weight heparin (LMWH) (**Table 2**), as well as unfractionated heparin. The optimal choice depends on the patient's comorbidities, renal function, and often financial and practical considerations, as well (eg, dosing frequency and route).

Acute Treatment

Typical options for initial treatment of DVT include the DOAC medications which can, but not necessarily need to, be preceded by parenteral anticoagulation (eg, LMWH). If choosing warfarin, initial parenteral anticoagulation is needed for at least 5 days until INR is >2.0 on two occasions that are 24 hours apart.[3] Options for parenteral bridging include heparin derivatives such as LMWH or unfractionated heparin (UFH).

Guidelines for anticoagulation recommend DOACs for most non–cancer-related DVTs, especially compared with warfarin. Meta-analyses have demonstrated evidence of lower rates of major and even fatal bleeding with DOACs compared with warfarin.[3] Furthermore, vs warfarin, DOACs have more predictable pharmacokinetics and rapid onset of action. Warfarin also requires frequent blood draws for monitoring of INR.

Certain clinical scenarios warrant use of specific anticoagulants (**Table 3**). In a study of 120 high-risk patients with antiphospholipid syndrome, warfarin was shown to have lower rates of thromboembolic events compared to rivaroxaban.[3] LMWH is the standard for patients with cancer. When compared with DOACs, LMWH has lower rates of major bleeding due to GI events. However, in non-GI cancers, DOACs are considered an acceptable alternative, showing noninferior effects on bleeding risks and even lower rates in recurrence.[3]

In the acute phase, isolated proximal DVTs are usually managed with 3 to 6 months of anticoagulation. If the isolated DVT occurs distally in calf, management options include a shorter course of (4-6 weeks) or even serial compression ultrasonography without starting anticoagulation for monitoring propagation of the clot.[10]

Chronic Treatment

Extension of treatment after the first 3 to 6 months usually depends on stratification based on risk of recurrence. The risk of recurrence is >3% in individuals with active cancer, active autoimmune disease, or antiphospholipid syndrome. For such patients, it is recommended to annually assess their risk of DVT and need for anticoagulation. Provoked DVTs also fall under this category of long-term anticoagulation; however, the characterization of provoked vs unprovoked DVTs is no longer used to determine length of treatment due to presence of predisposing factors. Postthrombotic syndrome or venous insufficiency occurs in 25% to 50% of patients at 3 to 6 months after diagnosis.[3]

In cases such as trauma resulting in fractures, minor surgery with anesthesia for more than 30 minutes, or acute illness resulting in immobility for more than 3 days, prolonged anticoagulation therapy is not warranted.[3]

Case Conclusion

When the Wells' score is applied, this patient gets 1 point for her pain along the deep venous system. Based on this, the patient has moderate risk with a 17% pretest probability.[7-9] Per current recommendations, the next step would be to complete a high-sensitivity D-dimer blood test. The patient has a negative high-sensitivity D-dimer testing completed in the urgent care. In moderate-risk patients with a negative high-sensitivity D-dimer by point-of-care testing, DVT can be ruled out with a negative predictive value of 96.1% and no further testing.[7-9] The patient is safely sent home with primary care follow-up. ■

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