CME: This article is offered for *AMA PRA Category 1 Credit*.™
See **CME Quiz Questions** on page 7.

Leg Pain in a 34-Year-Old Man

Urgent message: The ability to differentiate deep vein thrombosis from other diagnoses such as cellulitis is important in choosing the correct treatment option.

JEFF HEIMILLER, MD

Case Presentation

A 34-year-old male presented with a 1-week of right calf pain that was exacerbated by palpation and walking. He was unable to see his primary care physician that day, so he went to urgent care for evaluation. The patient also reported a sensation of shortness of breath since the onset of leg pain. He did endorse two previous hospitalizations for deep vein thrombosis and cellulitis, however the last admission for either was over 5 years ago. He is no longer taking anticoagulation. He reported his current pain did not feel quite the same as it did when he experienced DVT previously, and he denied calf edema, which was typical of previous episodes. The patient remembered that the initial pain and shortness of breath began when walking from his car to his office building. He further denied vomiting, diaphoresis, palpitations, syncope, edema, hemoptysis, cough, chest pain, leg trauma, and infectious symptoms such as fever.

©Fotolia.com

Vital signs

- Temp: 95.8° F
- Pulse: 67
- Resp: 20
- Blood pressure: 140/94
- Pulse ox: 99%

Past Medical History

- Medications: Ziac
- Allergies: NKDA
- PMH: HTN, DVT

Physical Examination

- General: Well-appearing, NAD, morbidly obese. A moderate-sized panniculus is present. A&O x3
- Head: Normocephalic; atraumatic
- Resp: Normal chest excursion with respiration; CTAB; no wheezes, rhonchi, or rales
- Card: RRR without murmurs, rubs, or gallops
- Abd: Morbidly obese, nontender to palpation, with no palpable organomegaly or masses
- Ext: Carotid, radial, femoral, and dorsalis pedis pulses are normal. Capillary refill normal. Peripheral edema: right and left calves are 61 cm and symmetrical, without obvious edema. No redness or warmth of the lower extremity. Positive for Homan's sign
- Skin: Normal for age and race; warm and dry; no apparent lesions

Results

- ECG: Normal sinus rhythm, rate of 75; normal ECG
- Venous Doppler: negative for DVT

Jeff Heimiller, MD is a Resident in the Department of Emergency Medicine at the Vanderbilt University Medical Center in Nashville, TN. The author has no relevant financial relationships with any commercial interests.

Diagnosis
1. Pain in limb, r/o DVT
2. Obesity
3. HTN

Disposition
- The patient was discharged to home ambulatory.

Primary Care Visit (1 Day Later)
Seen by PCP and sent for a V/Q, which showed multiple mismatched wedge-shaped perfusion defects. This includes two moderate-to-large subsegmental defects in the right lung base and one to two moderate-to-large subsegmental defects in the left lower lobe. There are also small subsegmental defects in the left upper and right upper lobes.

Impression
- High probability for pulmonary embolism.

Disposition
- Transferred to emergency department for admission to hospital.

Hospital Discharge Diagnoses and Discussion
1. Pulmonary embolus: Plan for anticoagulation and ECHO to evaluate for right ventricular strain
2. History of hypertension
3. Sleep apnea
4. Morbid obesity

Case Discussion: Evaluation of Lower Extremity Swelling and Pain
A patient presenting with isolated lower extremity swelling, palpable cords, Homan's sign, and a history of thromboembolic disease would raise even a medical student's suspicion for DVT.

Unfortunately for the provider, the presentation is often subtle. Congestive heart failure can result in lower extremity swelling and pain, but this is usually a bilateral presentation. Other causes of bilateral lower extremity swelling are obstructive processes at the level of the inferior vena cava (IVC), such as malignancy, pregnancy, and IVC thrombus. Traumatic processes, such as hematoma, muscle injury, or fractures are more likely to result in unilateral lower extremity swelling. It is often difficult to clinically distinguish DVT from cellulitis, as both often present with a diffusely swollen, painful, and erythematous lower extremity. However, certain findings such as ulceration, abscess formation, or lymphadenopathy are more specific to cellulitis. Prior DVTs can also result in destruction of normal venous anatomy, culminating in recurrent unilateral swelling.

Table 1. Wells Criteria for DVT[1]

Criteria	Score
Active cancer (patient receiving treatment for cancer within the previous 6 months or currently receiving palliative treatment)	1
Paralysis, paresis, or recent plaster immobilization of the lower extremities	1
Recent bedridden for >3 days or major surgery requiring general or regional anesthesia within the previous 12 weeks	1
Localized tenderness along the distribution of the deep venous system	1
Entire leg swollen	1
Calf swelling at least 3 cm larger than that on the asymptomatic leg (measured 10 cm below tibial tuberosity)	1
Pitting edema confined to the symptomatic leg	1
Collateral superficial veins (nonvaricose)	1
Previously documented deep vein thrombosis	1
Alternative diagnosis at least as likely as deep vein thrombosis	-2
Scores ≥ 2 qualify as high risk	

Physical exam is also tricky; while fairly specific, the presence of palpable cords is insensitive, and its absence should not be used to rule out DVT. Homan's sign is even less helpful; low sensitivity and specificity render it essentially meaningless in this regard. In contrast, comparing calf sizes remains one of the most specific physical exam findings in the evaluation of potential DVT. A difference of 3 cm in calf diameter measured 10 cm distal to the tibial tuberosity should greatly heighten one's suspicion for DVT.

The risk factors for DVT are many and variable, but they ultimately revolve around the triad of venous stasis, hypercoagulability, and endothelial injury first described by Virchow. The entire triad need not be present to result in DVT. Stasis resulting from immobility or paralysis, hypercoagulability resulting from malignancy or elevated estrogen levels, and endothelial injury resulting from recent trauma or instrumentation are all important examples of situations wherein a single derangement results in an increased risk of DVT. Wells, et al published a useful set of guidelines to help estimate an individual

Table 2. Modified Wells Prediction Rule for Diagnosing Pulmonary Embolism[3]

Criteria	Score
Clinical signs of deep vein thrombosis	3
Alternative diagnosis less likely than pulmonary embolism	3
Previous pulmonary embolism or deep vein thrombosis	1.5
Heart rate >100 beats per minute	1.5
Recent surgery or immobilization (within 30 days)	1.5
Hemoptysis	1
Cancer (treated within last 6 months)	1

Score 0-1 is low probability; 2-6 is intermediate probability; >6 is high probability.

Table 3. Pulmonary Embolism Rule-Out Criteria (PERC)[4]

- Age < 50
- HR < 100
- O2 sat on room air ≥ 95%
- No prior history of venous thromboembolism
- No surgery or trauma requiring hospitalization within 4 weeks
- No hemoptysis
- No exogenous estrogen
- No unilateral leg swelling

Note: All of the above must be present in order to apply PERC

patient's risk for DVT (**Table 1**).[1] However, this study does not specifically include certain high-risk groups such as pregnant women.

Using Patient History to Guide Evaluation of Potential Pulmonary Embolism

In contradistinction to the case presented, the potential for PE is not subtle in a patient presenting with sudden onset of pleuritic chest pain, dyspnea, and hemoptysis. Dyspnea related to PE, however, often develops much more insidiously, and may occur in the absence of chest pain. In fact, unexplained dyspnea is one of the strongest independent predictors of PE.[2]

Although a slow onset of dyspnea may mimic heart failure, this diagnosis is much more likely to cause orthopnea. In contrast, PE may even cause platypnea, where respirations are subjectively easier when supine. The varied characteristics of dyspnea in PE are often due to the specific location of the PE.

Pleuritic chest pain, which is one of the hallmark symptoms of PE, can be simply described as pain between the clavicles and the costal margin that is worse with deep breathing or cough. However, pain from PE may be referred to other parts of the body and in so doing, cause shoulder or high abdominal pain

Diagnosis of Pulmonary Embolism

In order to determine the most appropriate test to assess the potential risk for PE, it is helpful to first determine the patient's pretest probability for having a PE. Several decision instruments have been published to assist in risk stratifying. The modified Wells' score (**Table 2**) is one such risk stratification tool.[3] A widely accepted pretest probability cutoff to determine the need for further testing is <2%. It should be noted that once testing is performed, the commonly accepted cutoff for exclusion of PE is a posttest probability less than 1%.

In patients found to have a low pretest probability for PE, it may not be necessary to perform any laboratory testing or imaging. Kline, et al developed the PE rule-out criteria (the PERC rule), which is listed in **Table 3**.[4] If a patient is determined to have a low pretest probability and all criteria of the PERC rule are met, the risk of discharging that patient with a PE is <1.8%. Many advocate for using a Wells' score to determine which patients are low risk and then employing another validated instrument like the PERC to terminate a workup without having to employ a D-dimer if the PERC score is 0. In our patient's case, the history of DVT prevents application of the PERC rule, and we must proceed with further diagnostic testing.

Although a PE usually arises from a lower extremity DVT, a DVT is not always evident on the initial workup. For this reason, a negative ultrasound of the lower extremities does not rule out a PE. In fact, ambulatory patients are even less likely than hospitalized patients to have a discoverable DVT, making the lower extremity ultrasound an even less sensitive factor to exclude PE. In a best-case scenario, a negative Doppler ultrasound of the bilateral lower extremities results in a negative likelihood ratio of about 0.5—in other words, if a bilateral lower extremity Doppler is negative, this decreases your pretest risk by half.[5] Many have advocated for potentially using lower-extremity Doppler to reduce the radiation exposure in pregnant patients with concerns for PE. If the ultrasound is positive for DVT and the patient has a combined low pretest probability with a negative workup for submassive PE, then theoretically CT of the chest could be avoided.

The newer quantitative immunoturbidimetric or ELISA

D-dimer tests have a sensitivity and specificity of 95% and 50%, respectively, resulting in a negative predictive value of 0.1.[6] The D-dimer is thus an incredibly useful test in ruling out DVT in the low-to-moderate pretest probability groups. In fact, in moderate-risk patients or in low-risk patients who fail the PERC criteria, a negative D-dimer is sensitive enough to comfortably rule out PE. However, in the high-risk group, it is widely believed that the pretest probability is so great that the D-dimer is insufficient to rule out DVT without obtaining imaging of the pulmonary vasculature.

In our case, a ventilation/perfusion (V/Q) scan was used to make the ultimate diagnosis of PE, but this test has significant limitations. In general, only 50% of V/Q scans will result in a normal or diagnostic positive result,[7] with the other half resulting in "nondiagnostic" scans. These indeterminate results are usually the result of underlying lung disease, cardiovascular disease, or a chest x-ray that is significantly abnormal. Any baseline defect in ventilation or perfusion will limit the sensitivity of the VQ scan. When these nondiagnostic scans are read as low probability, the negative likelihood ratio is approximately 0.3, which may be enough to bring a low pretest probability patient into an acceptable range; however, further testing if often required, which is why many providers have begun to favor computed tomography.

Because of the vast improvements in quality of imaging with modern CT scanners, CT pulmonary arteriograms have become the test of choice. Adequate imaging and interpretation rely on an adequate injection technique and the radiologist's adeptness at reading the CT.

Management of Pulmonary Embolism

In determining the best means of managing a PE, it is helpful to first categorize how "large" or "serious" a PE is. Massive PE is defined as resulting in hemodynamic instability characterized by a systolic blood pressure <90 for 15 minutes or any persistent signs of shock.[8] Submassive PEs result in right ventricular dysfunction or myocardial necrosis, as evidenced by elevated troponin, elevated BNP or pro-BNP; ECG with evidence of right heart strain; CT with an enlarged right ventricle; or echocardiographic evidence of right heart strain, shock index <1, or a systolic blood pressure <90 at any time.[9] Both massive and submassive PEs should be referred immediately to an emergency department for further evaluation, as these may require emergent thrombolytics, mechanical intervention, or surgery.

"Initial anticoagulation with heparin remains the standard of care for low-risk PEs. Typically, patients will be started on unfractionated heparin or low molecular weight heparin as well as a vitamin K-dependent anticoagulant."

Although there is little real evidence to support its use, initial anticoagulation with heparin remains the standard of care for low-risk PEs. Typically, patients will be started on unfractionated heparin (UH) or low molecular weight heparin (LMWH), as well as a vitamin K-dependent anticoagulant such as warfarin at the time of diagnosis. Once a therapeutic INR of 2.0–3.0 has been reached, the follow-up provider can stop the heparin agent and the patient can be maintained on vitamin K antagonists for a period determined by their physician. The FDA has also approved several novel oral anticoagulants (NOACs), such as dabigatran, rivaroxaban, apixaban, and edoxaban for use in low-risk PEs. ■

References

1. Wells P, Anderson DR, Bormanis J, et al. Value of assessment of pretest probability of deep-vein thrombosis in clinical management. *Lancet*. 1997;350(9094):1795-1798.
2. Susec O, Boudrow D, Kline JA. The clinical features of acute pulmonary embolism in ambulatory patients. *Acad Emerg Med*. 1007;4(9):891-897.
3. Wells P, Anderson D, Rodger M, et al. Excluding pulmonary embolism at the bedside without diagnostic imaging: management of patients with suspected pulmonary embolism presenting to the emergency department by using a simple clinical model and d-dimer. *Ann Intern Med*. 2001;135(2):98-107.
4. Kline J, Mitchell A, Kabrhel C, et al. Clinical criteria to prevent unnecessary diagnostic testing in emergency department patients with suspected pulmonary embolism: *J Thromb Haemost*. 2004;2(8):1247-1255.
5. Daniel K, Jackson R, Kline J. Utility of lower extremity venous ultrasound scanning in the diagnosis and exclusion of pulmonary embolism in outpatients. *Ann Emerg Med*. 2000;35(6):547-554.
6. Kline J, Webb W, Jones A, Hernandez-Nino J. Impact of a rapid rule-out protocol for pulmonary embolism on the rate of screening, missed cases, and pulmonary vascular imaging in an urban US emergency department. *Ann Emerg Med*. 2004;44(5):490-502.
7. Roy PM, Colombet I, Durieux P, et al. Systematic review and meta-analysis of strategies for the diagnosis of suspected pulmonary embolism. *BMJ*. 2005;331:1–9.
8. Clark D, McGiffin D, Dell'Italia L, Ahmen M. Submassive pulmonary embolism where's the tipping point? *Circulation*. 2013;124(24):2458-2464.
9. Jaff M, McMurtry M, Archer S, et al. Management of massive and submassive pulmonary embolism, iliofemoral deep vein thrombosis, and chronic thromboembolic pulmonary hypertension: a scientific statement from the American Heart Association. *Circulation*. 2011;123(16):1788-1830.