



DISCLOSURES

None to
report



OBJECTIVES

- Examine the pathogenesis and risk factors of deep vein thrombosis and pulmonary embolisms.
- Use risk stratification scores to guide diagnostic studies and treatment plans in patient's at risk for a deep vein thrombosis and/or pulmonary embolisms.
- Incorporate evidence-based medicine in the diagnosis and treatment of deep vein thrombosis and pulmonary embolisms into clinical practice as applicable.



DEEP VEIN THROMBOSIS



DVT

- Risk Factors
 - *Venous stasis, endothelial damage, hypercoagulable states*
- Pathophysiology
 - *Accumulation of clotting factors and platelets that propagates proximally*
 - *Mobile thrombus can lead to PE*
 - *Rates of site involvement*
 - Distal veins 40%
 - Popliteal 16%
 - Deep femoral 20%
 - Common femoral 20%
 - Iliacs 4%



Venous stasis

Commonly caused by immobility (abdominal or lower extremity surgery and lower extremity casts), obesity, long-haul flights

Endothelial damage

Intravenous catheter placement, chemotherapy, vasculitis. Damage from previous DVT is most common cause of a second DVT

Hypercoagulable state

Inherited thrombophilias (factor V leiden mutation, antiphospholipid antibody, protein C or S deficiency), pregnancy, hormone replacement, oral contraceptives

This clot creates an obstruction to venous blood flow and the blood on the proximal side becomes stagnant allowing the clot to lengthen in a proximal direction.

If any portion of this clot that breaks free from the main body can travel to to the right heart and into the pulmonary circulation causing a pulmonary embolism.

DVT

- Clinical Manifestations
 - *May be asymptomatic*
 - *Pain, tenderness*
- Physical Exam
 - *Unilateral swelling*
 - Larger calf diameter is the greatest physical exam predictor
 - Calf or whole leg depending on location of clot
 - Possible + Homan's sign (unreliable)
 - *Skin discoloration – erythema, blue duskiness*
 - *Tenderness to palpation*
 - *Warmth, edema*



Typically present with non-specific symptoms of leg discomfort, throbbing or aching, or a sensation of warmth

Pain increases with ambulation and weight bearing

Wells Score

+1	Paralysis, paresis, or recent orthopedic casting of a lower extremity
+1	Recently bedridden (> 3 days) or major surgery within the past four weeks
+1	Localized tenderness in the deep vein system
+1	Swelling of an entire leg
+1	Calf swelling 3 cm greater than the other leg, measured 10 cm below the tibial tuberosity
+1	Pitting edema greater in the symptomatic leg
+1	Collateral nonvaricose superficial veins
+1	Active cancer or cancer treated within six months
-2	Alternative diagnosis more likely than DVT



If there is a suspicion of a DVT a clinical probability scoring set can be used to determine the patient's risk.

DVT

- Wells Score

- *The total score in an individual patient denotes their risk of DVT:*

- 0 points – Low probability; 3% risk of DVT
 - 1-2 points – Moderate probability; 17% risk of DVT
 - 3-8 points – High probability; 50-75% risk of DVT



Wells score has a high negative predictive value in patients with a low probability score for DVT (99.7%), but a lower negative predictive value in high risk patients (82%)

DVT

■ Diagnostic Studies

- *D-dimer level (normal <500 ng/mL)*
 - If positive, proceed to venous duplex
 - If negative, no additional testing is needed
- *Venous duplex ultrasound*
 - Demonstrates location and extent of thrombus
 - Shows acute vs chronic nature of clot
 - If clinical suspicion is high and the doppler was negative, a repeat study can be performed in 5-7 days.
- *Venography*
 - Used in rare cases such as when a cast cannot be removed or inconclusive ultrasound due to chronic venous scarring



D-dimer is a fibrin degradation product and is used as a surrogate marker of fibrinolysis. It is expected to be elevated during a thrombotic event, but can also be elevated in various conditions, such as pregnancy, postoperative state, and malignancy. Because of this a D-dimer test has a low specificity but a high sensitivity. Used in patient with low probability due to its greater negative predictive value

Ultrasound is the initial study in patients with moderate to high probability, or a secondary test in a low probability patient with an elevated D-dimer.

DVT

■ Treatment

- *The goal of therapy is to prevent clot propagation*
- *Proximal DVT*
 - Thrombus located in the popliteal, femoral, or iliac veins
 - Anticoagulant therapy is indicated for all patients with proximal DVT, regardless of the presence of symptoms.
- *Distal DVT*
 - Thrombus located below the knee in the peroneal, anterior tibial, or posterior veins
 - Anticoagulation is indicated in patients who are symptomatic.



Distal DVTs are most common in posterior tibial and peroneal veins, with anterior tibial and intramuscular vein DVTs uncommon findings

DVT

■ Treatment

- *Initial anticoagulation*

- IV UFH
- SQ LMWHs (enoxaparin [Lovenox]) or fondaparinux (Arixtra)
- PO factor Xa inhibitors: rivaroxaban (Xarelto) or apixaban (Eliquis)

- *Long-term anticoagulation*

- warfarin (Coumadin)
- Novel oral anticoagulants (NOACs)
 - dabigatran (*Pradaxa*)
 - rivaroxaban (*Xarelto*), apixaban (*Eliquis*)
- 3-6 months, depending on ultrasound surveillance



Long-term

Warfarin dose to keep INR between 2-3. Warfarin requires bridge therapy
Bridging therapy for dabigatran should be considered for patients at high risk of thrombosis; low-risk patients do not require bridging
Oxabans do not require bridging therapy
Plan for minimum of 3 months with extension of anticoagulants possible if venous duplex still shows clot burden

DVT

■ Treatment

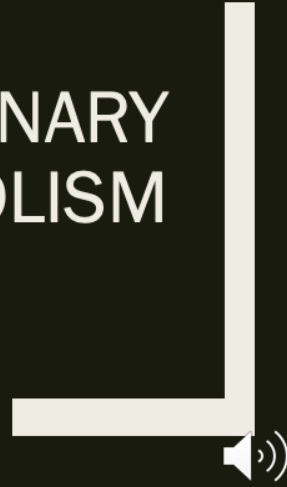
- *Thromboembolic deterrent (TED) stockings for lower extremity DVTs to prevent recurrence*
- *Thrombolysis*
 - Typically reserved for patients with extensive DVTs, affecting multiple veins.
- *Thrombectomy*
 - Patients with long DVTs, typically above the knee, that have an increased risk of mobilizing to the lungs.



Thrombolytics approved for DVTs include streptokinase, urokinase and tissue plasminogen activator. Thrombolytics are usually introduced via local IV or catheter directed infusion can be performed by an interventional radiologist.

Thrombectomy – vein is accessed proximal to the DVT and fogarty catheters are passed through the thrombus into the distal vein. When the fogarty catheter is removed the clot comes with it and can be removed from the vein.

PULMONARY EMBOLISM



PE

■ Pathophysiology

- *Blood flow through the lungs can be disrupted by several disorders that result in occlusion of the vessels, an increase in pulmonary vascular resistance, or destruction of the vascular bed.*
- *Widespread vasoconstriction, due to release of neurohumoral substances, further impedes blood flow to the lungs.*
- *The effect of the embolus depends on the extent of pulmonary blood flow obstruction, the size of the affected vessels, and the nature of the embolus.*
- *Results can vary between minimal functional significance to life threatening changes in ventilation-perfusion ratios.*



PE

- Most of the time a PE is caused by occlusion of a portion of the vascular bed by an embolus:
 - *Thrombus*
 - 90% of PEs are caused by DVTs from legs or pelvis
 - *Tissue fragment*
 - *Fat emboli*
- Risk factors
 - *Virchow's triad*
 - *Trauma*
 - *Surgery*



90% of PEs originate from DVTs of pelvic or lower extremity veins, and approximately 50% of DVTs may lead to a silent PE.

Trauma – pulmonary contusions, high impact trauma, trauma to the pulmonary vessels via indwelling catheters

PE

■ Clinical Manifestations

- *Classic presenting symptoms are pleuritic chest pain (39%) and dyspnea at rest (50%).*
- *Hemoptysis also is a common presenting complaint due to pulmonary infarction and can be seen in up to 20% of patients with PE.*
- *Unexplained anxiety*



Diagnosis of PE can be challenging because symptoms are nonspecific.

PE

■ Physical Exam

- *Tachycardia, tachypnea and/or hypoxia with a new or increasing oxygen requirement from baseline*
- *Lung sounds are often unremarkable though the patient may appear to be in respiratory distress*
- *Low-grade fever is less common*
- *Right ventricular dysfunction*
 - Hypotension and changes associated with shock
 - Elevated jugular venous pressure with a hepatojugular reflex
 - Pleural friction rub, RV heave, or a loud P2 may be noted if there is significant right heart failure



PE

■ Risk prediction calculators

- Wells criteria, revised Geneva score, and Pulmonary Embolism Rule-out Criterion (PERC)

PERC

Age \geq 50

HR \geq 100

Oxygen sats $<$ 95%

Unilateral leg swelling

Hemoptysis

Recent surgery or trauma (\geq 4 wks ago requiring general anesthesia)

Prior PE or DVT

Hormone use

If all criteria are negative, there is $<$ 2% risk of PE.

If any criteria are positive, the PERC cannot be used to rule out PE.

In the setting of a low-risk patient who is not PERC negative, a d-dimer should be considered.



Each aims to provide an objective method for estimating pretest probability of having a PE into low, intermediate, and high categories.

Of these prediction calculators, the Wells criteria has been most extensively studied and well validated. Prevalence of PE is only 1.3% in patients determined to be in the low-risk category based on Wells score.

The PERC has 8 criterion for patient consideration.

PE

■ Diagnostic Studies

- *D-Dimer* – great negative predictive value
- *Spiral Chest CT with contrast/CT pulmonary angiogram*
 - Most commonly used primary imaging method in patients with suspected PE due to decreased invasiveness and speed of test results.
 - Spiral CTs has largely replaced the traditional gold standard of pulmonary angiography.
- *Ventilation-perfusion (V/Q) scan*
 - Typically reserved for patients with contraindication to a spiral CT, such as individuals with dye allergies or CKD.



D-dimer

In combination with a low pretest probability for PE, a normal D-dimer has been shown to rule out PE due to its high sensitivity (80%–100%) and negative predictive value up to 99%.

Spiral CT

Single detector spiral CT has a sensitivity of ~85–90% and a specificity between 88–95%.

Even when it is negative, it can be helpful in identifying other etiologies responsible for hypoxic respiratory failure, such as interstitial lung disease, pneumonia, or effusion.

When spiral CTs was compared with conventional pulmonary angiography in a meta-analysis, the rate of venous thromboembolism diagnosis after a negative spiral CT was no different from that of pulmonary angiography. Limitations of the method include a decreased sensitivity for the detection of small isolated clots in the peripheral pulmonary arterial bed, and a potentially reduced image quality in patients with coexistent cardiopulmonary disorders.

V/Q scan

High sensitivity and high specificity. V/Q scan is more sensitive in diagnosing chronic PE than spiral CT(97.4% vs 51%).

PE

- Classifications

- *American Heart Association (AHA) and American College of Chest Physicians (ACCP)*

- Massive PE is persistent hypotension of SBP < 90 mm Hg lasting more than 15 minutes or requiring inotropic support, pulselessness, or bradycardia less than 40 beats per minutes.
 - Submassive PE is a PE without systemic hypotension (SBP >90 mm Hg) but with RV dysfunction. RV dysfunction is based on either imaging (spiral CT or transthoracic echocardiogram) or elevated biomarkers (BNP or troponin).
 - Low-risk PE is an acute PE without hemodynamic instability and without RV dysfunction.



PE

■ Treatment

- *All patients with high pretest probability or confirmed PE should be initiated on anticoagulation.*
- *Anticoagulants*
 - IV UFH or SQ enoxaparin (Lovenox) or fondaparinux (Arixtra).
 - Novel oral anticoagulants (NOACs) are the preferred agent of choice over vitamin K antagonists (VKAs) for outpatient therapy.
 - Treat for 3 months and longer if D-dimer levels remain elevated.



Empiric early anticoagulation has been associated with decreased mortality for patients with acute PE.

When untreated, VTE can have a mortality up to 25% but decreases to 1% to 5% with treatment.

PEs accounts for approximately 5% to 10% of deaths in hospitalized patients.

Anticoagulants

Initial meds - Studies have shown there is no difference between using either of these, but LMWH is favored due to ease of monitoring.

PE

- Treatment

- *Thrombolytic agents*

- Patients with cardiac arrest or hemodynamic instability
- Systemic vs catheter-directed
- Approved thrombolytics for PE include alteplase (tPA), urokinase, and streptokinase.

- *Pulmonary thrombectomy*

- A surgical embolectomy should be considered in patients with a massive PE or patients with submassive PEs who are not candidates for systemic thrombolytics.



For patients who present with cardiac arrest or hemodynamic instability, it is widely accepted that reperfusion strategies should be initiated. Systemic thrombolysis, however, is not without risk; studies show a 20% risk of major bleeding events and a 3% risk of intracranial hemorrhage after receiving thrombolytics.

PE

- Treatment

- *IVC filter placement*

- Reserved for patients with intolerance or contraindications for anticoagulant therapy.
 - Case by case basis for patients with recurrent PEs, or DVTs despite anticoagulant treatment.
 - The American College of Chest Physicians recommends the use of retrievable filters, with every attempt being made to remove the filter when no longer indicated.



Studies have shown limited benefit of IVC filters in patients with acute PE or DVT to prevent future recurrent VTE events.

PE

PE Severity Index (PESI)	
Age	Age in years
Male gender	+ 10 points
History of cancer	+ 30 points
History of chronic lung disease	+ 10 points
History of heart failure	+ 10 points
HR > 110 bpm	+ 20 points
SBP < 100 mmHg	+ 30 points
RR > 30 bpm	+ 20 points
Temperature < 36°C/96.8°F	+ 20 points
Altered mental status	+ 60 points
Oxygen sats < 90%	+ 20 points

Risk groups


Very low ≤ 65

Low 66-85

Intermed 86-105

High 106-125

Very high >125



The PE severity index (PESI) is commonly used to predict short-term morbidity and mortality with PE.

These scores were derived from 11 patient factors associated with a 30-day mortality. Patients are risk stratified and management strategies are tailored to the risks of adverse outcomes.

The PESI has a high sensitivity and negative predictive value of 95-99% for predicting short-term outcomes.

Multiple studies have demonstrated that patients with low PESI scores had mortality less than 1% compared with high PESI group patients who had a 24% 30-day mortality.

If the patient is considered very low (≤ 65) or low risk (66-85) by the PESI score. They have an overall low risk of mortality or severe morbidity and OP management can be considered if clinically appropriate and social factors allow for it.

If the patient is considered intermediate (86-105), high (106-125) or very high risk (>125) by the PESI than higher levels of care, such as ICU placement, should be considered due to overall high risk of mortality and severe morbidity.

RESOURCES

- Thacil J. Deep vein thrombosis. *Hematology*, 2014; 19 (5): 309-310.
- Stubbs MJ, Mouyis M, Thomas M. Deep vein thrombosis. *BMJ*, 2018; 360: k351.
- Herold CJ. Spiral computed tomography of pulmonary embolism. *Eur Respir J*, 2002; 19:13s-21s.
- Albertsen IE, Goldhaber SZ, Piazza G, Overvad TF, Nielsen PB, Larsen TB, Søgaard M. Predictors of not initiating anticoagulation after incident venous thromboembolism: a Danish nationwide cohort study. *Am J Med*. 2019; doi: 10.1016/j.amjmed.2019.08.051.
- Essien EO, Rali P, Mathai SC. Pulmonary embolism. *Med Clin North Am*. 2019 May;103(3):549-564.



RESOURCES

- van Maanen R, Rutten FH, Klok FA, Huisman MV, Blom JW, Moons KGM, Geersing GJ. Validation and impact of a simplified clinical decision rule for diagnosis pulmonary embolism in primary care: design of the PECAN prospective diagnostic cohort management study. *BMJ Open*. 2019;9(10):e031639.
- Porres-Aguilar M, Anaya-Ayala JE, Jiménez D, Mukherjee D. Pulmonary embolism response teams: pursuing excellence in the care for venous thromboembolism. *Arch Med Res*. 2019;50(5):257-258.
- Kajy M, Mathew A, Ramappa P. Treatment failures of direct oral anticoagulants. *Am J Ther*. 2019 Oct 9. doi: 10.1097/MJT.0000000000001083.

BRI KESTLER, PA-C

bri.kestler@gmail.com

