Coagulation Process, Diagnosis of PE, and Incidence of PE

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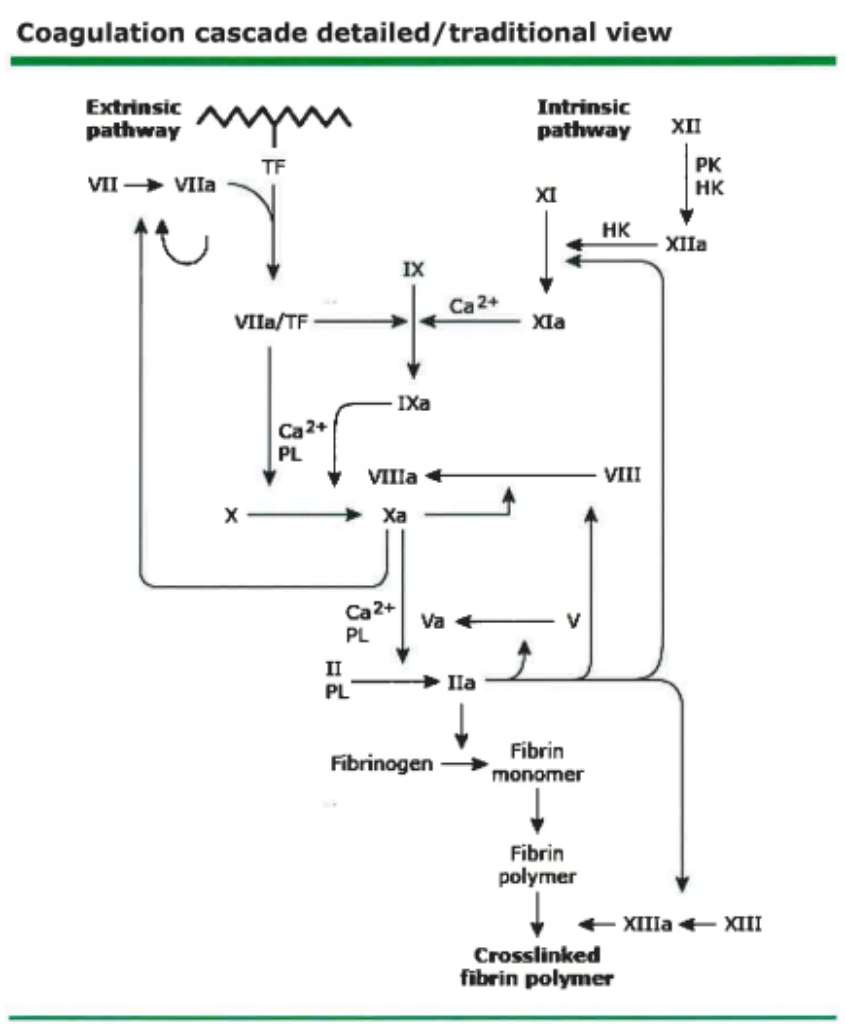
Rajan Memorial Lecture January 9th, 2022

Coagulation Cascade



Incidence of Pulmonary Embolism (PE)

The incidence of PE ranges from 39 to 115 per 100,000 annually. It is the third most common type of cardiovascular disease, following coronary artery disease and stroke. Just like DVT, PE occurs in males more than in females.

The mortality rate is high, causing 100,000 deaths in the U.S. every year. However, it is challenging to estimate this number accurately. The case fatality rates of PE have been decreasing, most likely due to the improvement of diagnostic methods, the initiation of early intervention, and better medicine.

Diagnostic Workup

The diagnostic workup for PE is very thorough and includes many different tests and analysis. Some are an arterial blood gas (ABG) analysis, checking brain natriuretic peptide (BNP) levels, checking troponin levels, D-dimer testing, electrocardiography (ECG), a chest radiograph (CXR), computed tomographic pulmonary angiography (CTPA), lung scintigraphy, pulmonary angiography, magnetic resonance angiography, echocardiography, and compression ultrasonography (US). Additionally, the Geneva Clinical Prediction rule and the Wells Criteria are used to find the risk level and probability for PE and estimate the pretest probability. The Pulmonary Embolism Rule-out Criteria is also used to select patients with such low likelihood of PE that diagnostic workup should not even be initiated.

Arterial Blood Gas Analysis

An ABG analysis measures the acidity and levels of oxygen and carbon dioxide in the blood from an artery. In an ABG analysis:

- Unexplained hypoxemia with a normal chest radiograph should raise suspicion

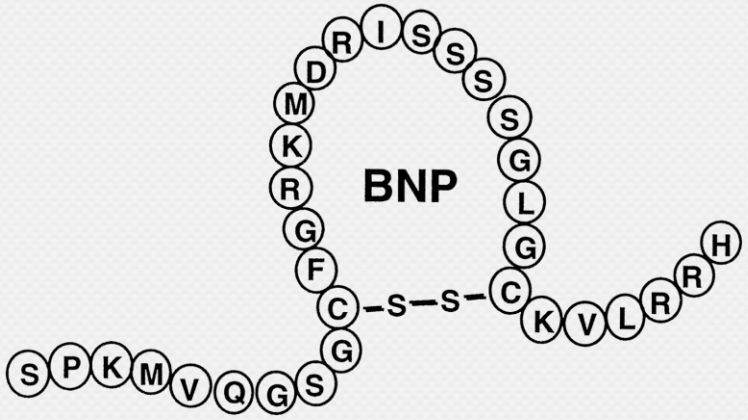
Commonly seen findings on an ABG analysis that are pathophysiological responses of PE:

- widened alveolar-arterial gradient for oxygen
- respiratory alkalosis
- hypocapnia

Note: hypercapnia, respiratory, or lactic acidosis are not common but can be found in PE patients.

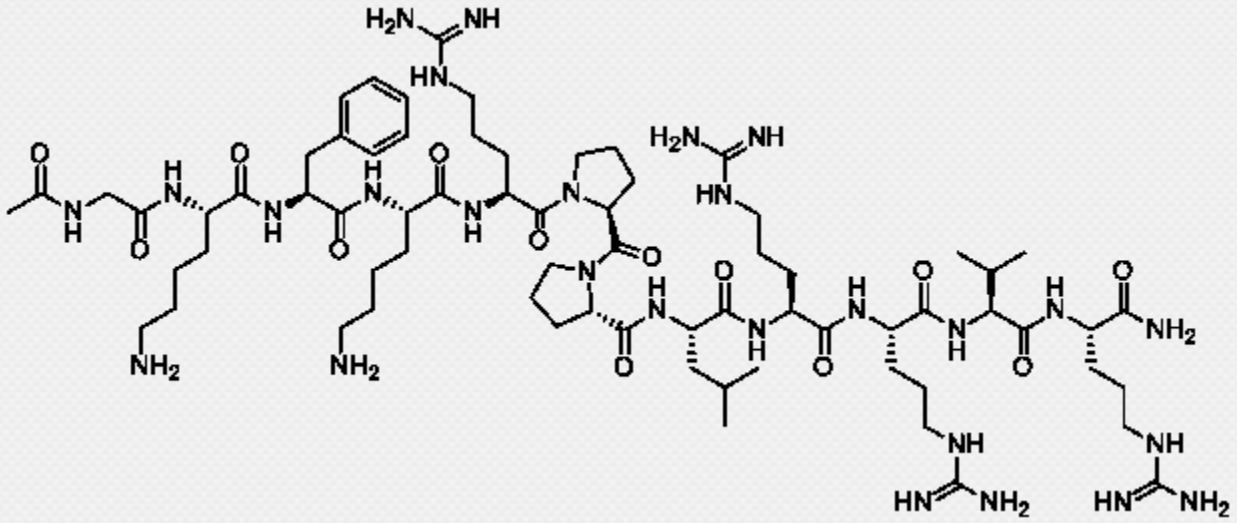
Brain Natriuretic Peptide

Although limited, elevated BNP levels have some diagnostic importance in PE patients. This is because right ventricle pressure overload due to acute PE is associated with more myocardial stretch, which then releases BNP and (NT)-proBNP. This means that the level of natriuretic peptides in blood reflect the severity of right ventricle dysfunction in acute PE.



Troponin

Although not diagnostically, serum troponin I and T levels are beneficial prognostically. Troponin levels are markers of right ventricle dysfunction and are elevated in 30 to 50 percent of patients with moderate to large PE. They are linked to clinical deterioration and death after PE.



D-dimer Testing

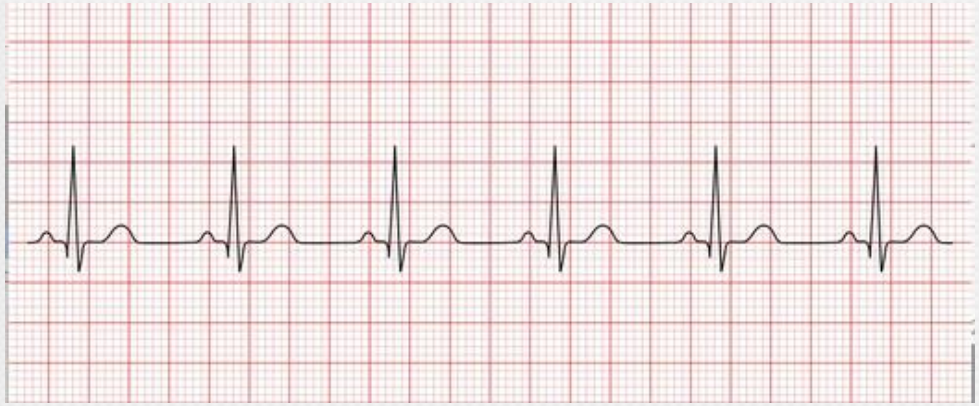
D-dimer tests look for D-dimers (protein fragments caused when blood clots are dissolved in the body) in blood. Because of the activation of coagulation and fibrinolysis pathways at the same time whenever there is an acute thrombosis process in the body, D-dimer levels are elevated in plasma.

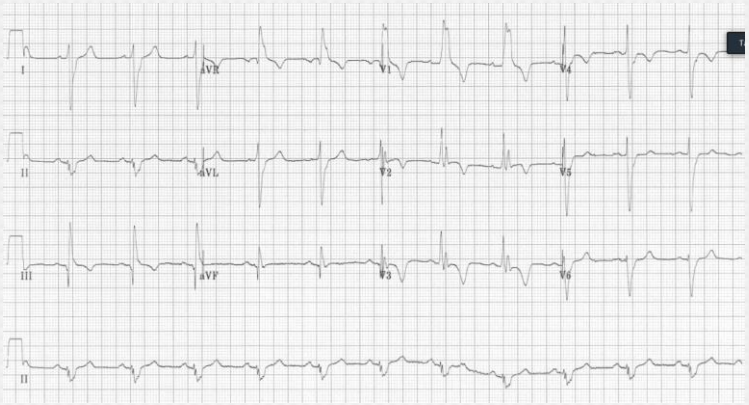
D-dimer testing has high negative predictive value, so a normal D-dimer level makes acute PE or DVT unlikely. However, D-dimer testing is not useful for the confirmation of PE, since the positive predictive value of elevated D-dimer levels is low.

Electrocardiography

The most common ECG findings in PE are tachycardia and nonspecific ST-segment and T-wave changes.

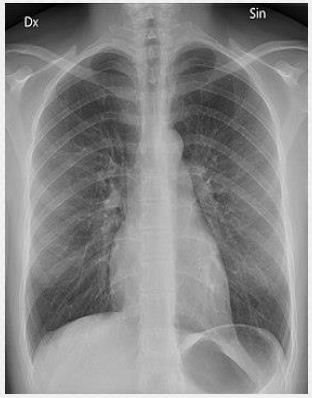
S1Q3T3 pattern, right ventricular strain, and new incomplete right bundle branch block are uncommon.

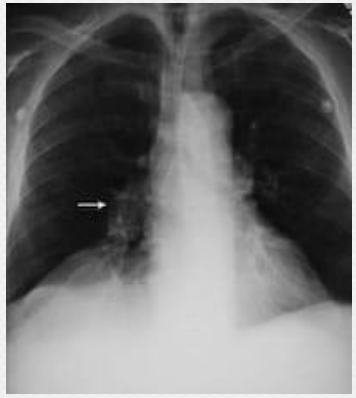




Chest Radiograph

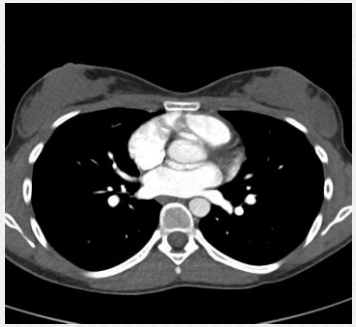
CXR in PE patients is usually normal or might show nonspecific abnormalities such as atelectasis or effusion. However, this is still useful, as it can be used to rule out alternative diagnoses in patients presenting with acute dyspnea. Hampton's hump and Westermark's sign are two rare but specific findings from a CXR that indicate acute PE.

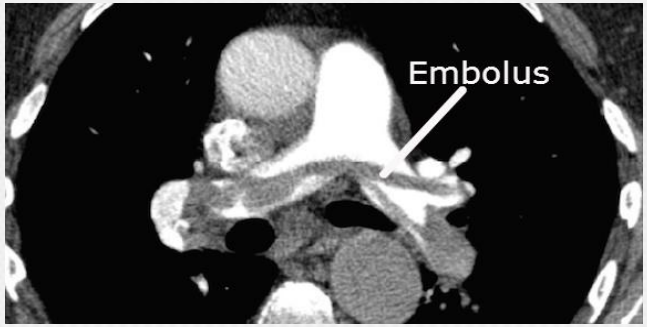




Computed Tomographic Pulmonary Angiography

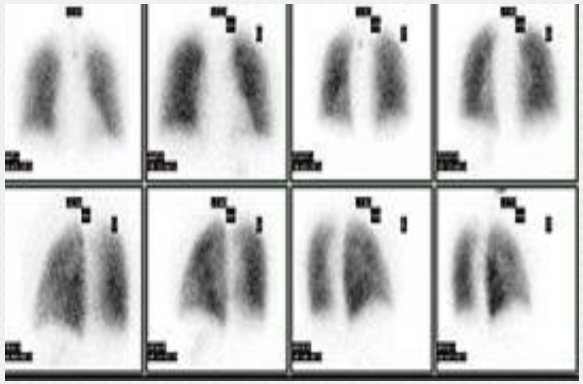
Multidetector CTPA is the preferred diagnostic modality for patients with suspected PE. It allows appropriate visualization of the pulmonary arteries down to the subsegmental level. A negative CTPA result is adequate for the exclusion of PE in patients who have a low or intermediate clinical probability. CTPA can also detect RV enlargement and other indicators of RV dysfunction.

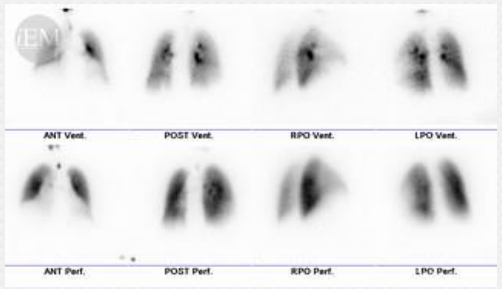




Lung Scintigraphy

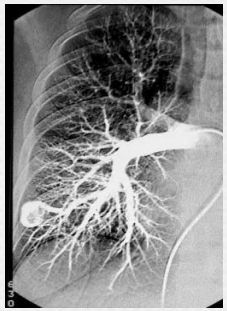
The planar ventilation/perfusion scan (V/Q scan) is an established diagnostic test for suspected PE. V/Q scanning is mostly performed for patients in whom CTPA is contraindicated or inconclusive, or when additional testing is needed. However, a normal chest radiograph is usually required before V/Q scanning, because scans performed on patients with abnormal chest radiographs are most likely to be false positives. V/Q scanning is the test of choice for the diagnosis of PE in pregnancy as well as other patients. Planar lung scan results are frequently classified into three-tiers: normal, high-probability, and nondiagnostic scans.

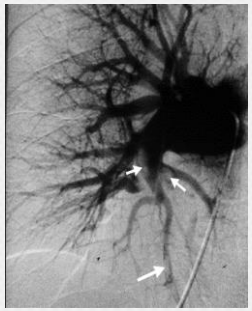




Pulmonary Angiography

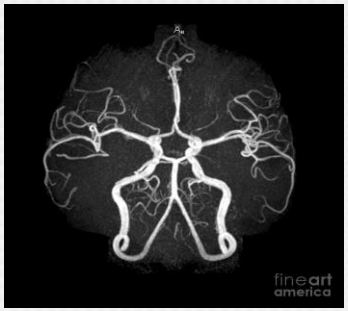
In pulmonary angiography, contrast is injected via a catheter introduced into the right heart under fluoroscopy. In the past, this was the gold standard for PE diagnosis. The diagnosis of acute PE is made on the evidence of a thrombus either as amputation of a pulmonary arterial branch or filling defect. However, ever since the widespread emergence of CTPA, pulmonary angiography is rarely used and reserved for rare circumstances for patients with a high clinical probability of PE, since CTPA or V/Q scanning would then be nondiagnostic. Pulmonary angiography results are operator dependent and highly variable, making the process inferior to CTPA.

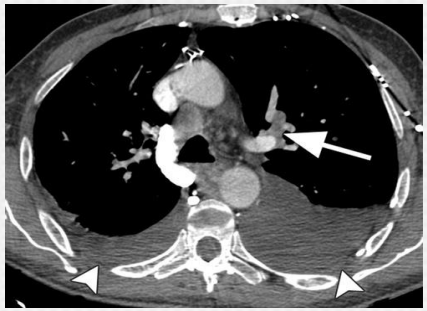




Magnetic Resonance Angiography

For many years, MRA has been assessed for several years regarding suspected PE. However, the results of large-scale studies show that this technique, although promising, is not recommended as a first-line test for the diagnosis of PE. This is because of its due to its low sensitivity, low availability in most emergency settings, and tendency to have a high proportion of inconclusive scans. MRA scans can still be used in patients in whom neither CTPA nor V/Q scan can be performed. The potential advantages include suffering no exposure to radiation.



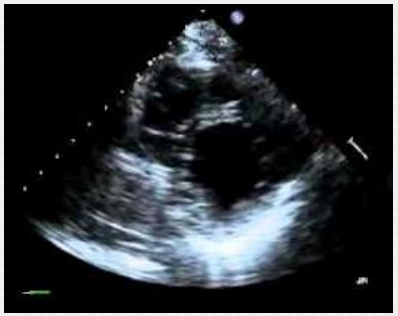


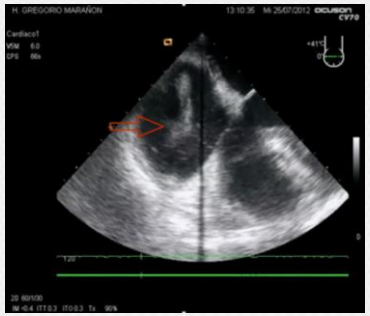
Echocardiography

Very rarely, transthoracic echocardiography can diagnose PE definitively, if the thrombus is visualized in the proximal pulmonary arteries. The diagnosis of PE on echocardiography is supported by the presence of clot in the right heart or new right heart strain.

There are significant considerations with using echocardiography to establish a diagnosis of PE. Due to the peculiar shape of the RV, there is no single echocardiographic parameter that gives quick and accurate information on RV size or function.

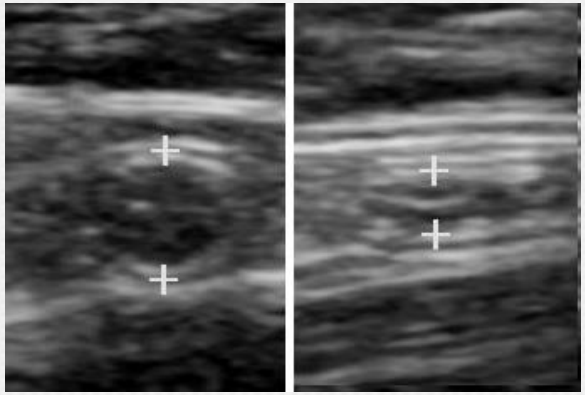
Additionally, the negative predictive value means that a negative result cannot exclude PE.

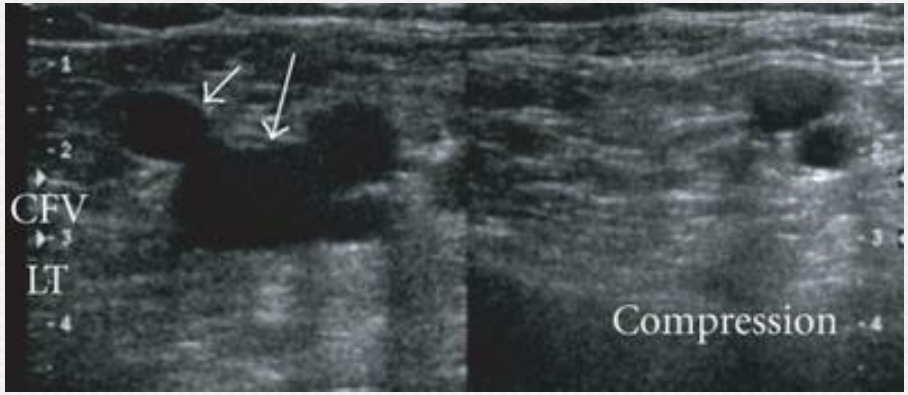




Compression Ultrasonography

PE originates from a lower limb DVT in a majority of patients. Therefore, a finding of proximal DVT in patients suspected of having PE is considered sufficient to warrant anticoagulant treatment without further testing. However, the low sensitivity of compression ultrasonography means that it should only be used if tests like CTPA or V/Q scanning are indeterminate.





Wells Criteria, Geneva Clinical Prediction Rule, and Pulmonary Embolism Rule-out Criteria

The Wells Criteria and Geneva Clinical Prediction Rule are scoring systems most commonly used to estimate the pretest probability of having a PE.

This allows the classification of patients with suspected PE into categories of clinical or pretest probability, based on which the diagnostic tests are chosen and interpreted.

The Pulmonary Embolism Rule-out Criteria is another set of criteria used to select patients with such low likelihood of PE that diagnostic workup should not even be initiated.

Wells Scoring System

The Wells Scoring System takes clinical symptoms of DVT, other diagnoses less likely than pulmonary embolism, heart rate >100 beats per min, immobilization for three or more days or surgery in the previous four weeks, previous history of DVT, hemoptysis, and malignancy into account. It has a 3 level scoring system:

- Low: <2.0
- Moderate: 2.0-6.0
- High: >6.0

Geneva Clinical Prediction Rule

The Geneva Clinical Prediction Rule works similarly and takes previous PE or DVT, heart rate, surgery or fracture within the past month, hemoptysis, active cancer, unilateral lower-limb pain, pain on lower-limb deep palpation and unilateral edema, and age into account. It also has a 3 level scoring system:

- Low: 0-3 / 0-1
- Intermediate: 4-10 / 2-4
- High: ≥11 / ≥5

Conclusion

- There are a plethora of diagnostic methods used for PE. Some, like computed tomographic pulmonary angiography and planar ventilation/perfusion scanning, are used before other tests.
- For patients with a high clinical probability of PE, these tests would be indeterminate or nondiagnostic, meaning the other diagnostic methods could be used.
- Most approaches will combine clinical and pretest probability assessments, D-dimer testing, and definitive diagnostic testing. Depending on the circumstances of the patient, different tests will be selected