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Review Article

REVIEW ON PULMONARY EMBOLISM

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ABSTRACT

Pulmonary Embolism occurs when blood clots break off from vein walls and travel through the heart to the pulmonary arteries of lungs that might have travelled from mostly legs or other parts of body to lungs through bloodstream. As pulmonary embolism derives blood clot in legs called deep vein thrombosis, which is also known as venous thromboembolism. Symptoms include shortness of breath, chest pain, cyanosis and rapid heart rate. Symptoms of a blood clot in the leg may also be present such as a red, warm, swollen, and painful leg. Diagnosing PE can be challenging. Various resources are available, such as clinical scoring systems, laboratory data, and imaging modalities that guide clinicians in their work-up of PE. Prompt recognition and treatment are essential for minimizing the mortality and morbidity associated with PE. Advances in recognition and treatment have also enabled treatment of some patients in the home setting and limited the time of hospital stay. This article will review the risk factors, pathophysiology, clinical presentation, evaluation, diagnosis, and treatment of pulmonary embolism.

Keywords: Pulmonary Embolism, Duplex ultrasound, Computed Tomography, Pulmonary Angiogram, Ventilation perfusion scan.

INTRODUCTION

Pulmonary embolism, first described by Virchow in the 1800s, was often a terminal event. A 1960 Pulmonary embolism (PE) is a common, treatable, highly lethal emergency, which despite advances in diagnostic testing, remains an under diagnosed killer. The mortality rate of diagnosed and treated pulmonary embolism ranges from 3-8%, but increases to about 30% in untreated pulmonary embolism. PE is a part of the spectrum of venousthromboembolic disease and most pulmonary emboli have their origin from clots in the iliac, deep femoral or popliteal veins. Nonspecific clinical signs and symptoms with low sensitivity and specificity of routine tests such as arterial blood gas, chest roentgenogram and electrocardiogram make the diagnosis of PE very challenging for the clinician. Pulmonary angiography is the gold standard diagnostic test, but this technique is invasive, expensive, not readily available and labor intensive. Diagnostic strategies have revolved around establishing clinical probabilities based on predictive models, then ruling in or ruling out the diagnosis of PE with various tests. Key trial on the efficacy of heparin in pulmonary embolism found a mortality rate of 17% Venous thromboembolism (VTE) and PE is the third most common cause of cardiovascular death after myocardial infarction (MI) and cerebrovascular accidents (CVA) [1]. Many PEs are likely undiagnosed and calculating the true incidence remains challenging. However, PE remains a significant cause of preventable in hospital mortality.

Risk Factors:

Most clinically significant PEs originate as venous thromboembolism is in the lower extremities or pelvic veins. Less frequently upper extremity thromboembolic events lead to PE. Various conditions lead to the development of VTE. Virchow's triad of hypercoagulability, venous stasis and vessel wall injury provides a model for understanding many of the risk factors. Major joint surgery, multiple trauma, abdominal surgery, pelvic surgery, chronic heart failure with MI, these factors are usually either inherited or acquired as shown in Tables 1 and 2.

Weak	Medium	Strong
Hyperhomocy-steinemia	Mutation in the factor V Leiden (FVL)	Deficiencies of coagulation inhibitors including antithrombin (AT), protein C (PC), and its cofactor protein S (PS)
	Mutation in the 3′-untranslated part of the prothrombin (Factor II) gene (prothrombin 20210A, rs 1799963)	Insufficiency of anticoagulant pathways such as tissue factor pathway inhibitor (TFPI), thrombomodulin and endothelial protein C receptor (EPCR)
	Blood group (non-O blood group)	Elevated level of factor VIII
	C- to T-variation at position of 10034 in the fibrinogen gamma chain (rs 2066865)	

Table 1: Inherited Risk Factors for VTE [2, 3]

WEAK (odds ratio <2)	MEDIUM (odds ratio 2–9)	STRONG (odds ratio >10)
Bed rest (>3 days)	Arthroscopic knee surgery	Fracture (hip or leg)
Extended immobility (air travel >8 hours)	Central venous lines	Hip or knee replacement
Increasing age (³40 years	Chemotherapy	Major general surgery
Laparoscopic surgery	Congestive heart or respiratory failure	Major trauma
Obesity	Hormone replacement therapy or oral contraceptive therapy	Spinal cord injury
Pregnancy/antepartum	Malignancy	
Varicose veins	Pregnancy/postpartum	
	Previous VTE	

Table 2: Acquired Risk Factors for VTE [2-4]

Overall, major risk factors for thromboembolic events include recent immobilization, MI, CVA, surgery, and recent trauma. Additional major risk factors include prior VTE, advanced age, malignancy, known thrombophilia, and indwelling venous catheter. Moderate risk factors include family history of VTE, use of estrogen or hormone replacement therapy, smoking, pregnancy and obesity.,

Pathophysiology:

Pulmonary embolism occurs when deep venous thrombi detach and embolize in the pulmonary circulation. Pulmonary vascular occlusion occurs and impairs gas exchange and circulation. In the lungs, the lower lobes are frequently affected than the upper with bilateral lung involvement being common. Larger emboli wedge in the main pulmonary artery, while smaller emboli occlude the peripheral arteries. Peripheral

Pulmonary embolism can lead to pulmonary infarction, manifested by intra-alveolar hemorrhage. Pulmonary infarction occurs in about 10% of patients without underlying cardiopulmonary disease. Obstruction of the pulmonary arteries creates dead space ventilation as alveolar ventilation exceeds pulmonary capillary blood flow. This contributes to ventilation-perfusion mismatch, with vascular occlusion of the arteries increasing pulmonary vascular resistance. In addition, humoral mediators, such as serotonin and thromboxane are released from activated platelets and may trigger vasoconstriction in unaffected areas of lung. As the pulmonary artery systolic pressure increases, right ventricular after load increases, leading to right ventricular failure. As the right ventricular failure progresses, impairment in left ventricular filling may develop. Rapid progression to myocardial ischemia may occur secondary to inadequate coronary artery filling with potential for hypotension, syncope, electromechanical dissociation or sudden death.

Clinical Presentation:

Prompt recognition of a pulmonary embolism is crucial because of the high associated mortality and morbidity, which may be prevented with early treatment. Failure to diagnose pulmonary embolism is a serious management error since 30% of untreated patients die, while only 8% succumb with effective therapy. Unfortunately, pulmonary embolism may be asymptomatic or present with sudden death. Characteristic signs and symptoms such as tachycardia, dyspnea, chest pain, hypoxemia, and shock are non-specific and are present in many other conditions, such as acute MI, congestive heart failure or pneumonia. In the Prospective investigation of pulmonary embolism Diagnosis II (PIOPED II) trial, patients with pulmonary embolism had a range of signs and symptoms. Common signs were tachypnea (54%) and tachycardia (24%). The most common symptoms were dyspnea, usually of onset within seconds, at rest or with exertion (73%), pleuritic pain (44%), calf or thigh pain (44%), calf or thigh swelling (41%), and cough (34%)[5]. With only 24% of patients presenting with tachycardia, the majority of patients lacked one of the most common findings. Additionally, PIOPED II excluded many types of patients, such as those with chronic elevated creatinine levels or receiving dialysis, critically ill patients, or people with recent MI. Applicability is therefore limited. Therefore, a high index of suspicion and assessment of risk factors are critical for the recognition of pulmonary embolic events.

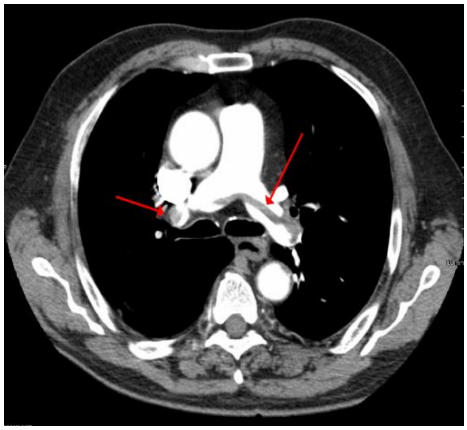

Figure 1

Axial Contrast Ct scan of chest showing multiple filling defectsat the bifurcation ("saddle" pulmonary embolism) and in bilateral pulmonary arteries.

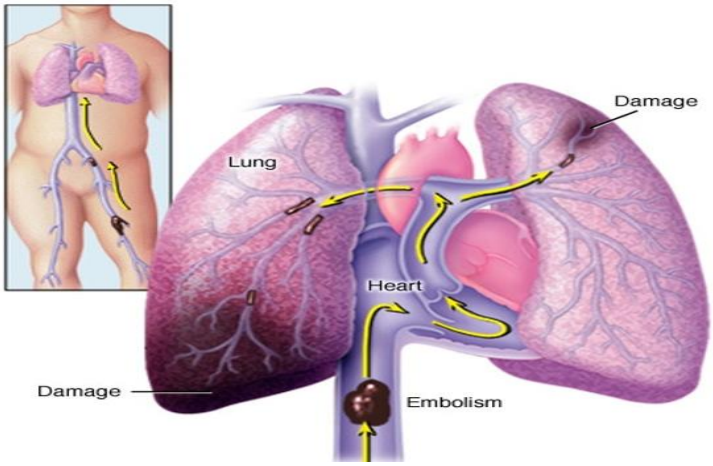

Figure 2

Pulmonary embolism occurs when a blood clot gets lodged in an artery in the lung, blocking blood flow to part of the lung. Blood clots most often originate in the legs and travel up through the right side of the heart and into the lungs.

Evaluation:

Because of the variable nature of the presentation of pulmonary embolism, the evaluation largely depends on the likelihood of pulmonary embolism and the stability of the patient. There are scoring systems to assist in the determination of likelihood of pulmonary embolism and thromboembolic events. Diagnostic scoring systems such as the Wells criteria and Geneva score Table 3 and Table 4.

Symptoms and signs of deep-vein thrombosis	3.0
Heart rate >100 beats per minute	1.5
Recent immobilization or surgery (<4 weeks)	1.5
Previous PE or deep venous thrombosis (DVT)	1.5
Hemoptysis	1.0
Active cancer	1.0
PE more likely than alternate diagnosis	3.0
Total score:	
</= 4 PE unlikely	
>4 PE likely	

Table 3: Modified Wells criteria

Previous DVT or PE	3
Heart Rate	
75–94 beats/min	3
>/=95 beats/min	5
Surgery or fracture within 1 month	2
Hemoptysis	2
Active Cancer	2
Unilateral lower limb pain	3
Pain on lower limb deep venous palpation and unilateral edema	4
Age >65 years	1
Total score:	
</= 5 PE unlikely	
>5 PE likely	

Table 4: Revised Geneva score

If a patient fulfills all of the PERC criteria and has a low probability of PE by Wells criteria and the gestalt opinion of the evaluating physician, then a PE may be ruled out [6]. In reality, very few patients meet these criteria and the PERC assessment is not reliable for the patient in hospital setting. The aforementioned tools: Wells score, Geneva score, and PERC work best in assessing the need for further work-up of stable patients presenting to the emergency room; with inpatients and critically ill patients, such tools are not as reliable. The elements of diagnostic workup will vary depending on whether the patient is hospitalized and whether there is hemodynamic instability in a patient with a suspected pulmonary embolism.

Diagnosis of proximal DVT in a symptomatic patient, or in an asymptomatic patient who has contraindications to CT angiography, is sufficient to rule in Pulmonary embolism[7]. In a stable patient,

presenting from an outpatient setting, who has not sustained recent trauma or surgery, a d-dimer test should be performed. If negative and clinical suspicion is low, then the likelihood of PE is low and further workup is unnecessary. D-Dimer is a degradation product of cross-linked fibrin that is formed immediately after fibrin clots are degraded by plasmin and reflects a global activation of blood coagulation and fibrinolysis. Therefore, d-dimer is not a useful test in post-operative patients because it will be elevated due to coagulation and fibrinolysis. It is also elevated in trauma patients, hospitalized patients and those with critical illness for similar reasons. Extremity venous ultrasound (US) is a quick, noninvasive modality that can detect DVT. As it can be performed with a portable machine, venous US may avoid the need for potentially dangerous transport of unstable, critically ill patients. Unfortunately, US testing often depend on the availability of technicians to perform the imaging and further evaluation by radiologists and other physicians with such skills. Recently, emergency room physicians and intensivists have been trained in US who results in faster detection of both symptomatic and asymptomatic extremity thromboses. When performed by trained ICU physicians, compression US studies of the extremities yielded a sensitivity of 86% and a specificity of 96% with a diagnostic accuracy of 95%[8]. In this same trial, median time delay between the ordering of formal vascular study (FVS) and the FVS result was 13.8 hours, which leads to significant delays in treatment. In another study, after 10 minutes of training in two point compression ultrasound, emergency medicine physicians were able to detect lower extremity thrombosis with a sensitivity of 100% and a specificity of 99% [9]. Besides the limitations of time delay due to lack of available personnel to perform such imaging, there are certain patient limitations that may limit study accuracy and feasibility; obesity, edema, and dressings often impede good imaging quality[10]. The other consideration in obtaining lower extremity ultrasound for diagnosis of Pulmonary embolism is that it is not a reliable modality to check for pelvic venous thrombosis and there are also many instances in which patients have PEs, but no evidence of extremity thrombosis. In one study, the use of ultrasonography alone for suspected PE had a sensitivity of only 29%[11]. Furthermore, false positive results may result in potentially dangerous and unnecessary anticoagulation in patients who do not actually have PEs. Helical CT angiography has largely replaced ventilation perfusion (V/Q) lung scanning for diagnosis because it is rapid, permits direct visualization of PE and can demonstrate other diagnoses in patients without PE. In patients with a contraindication to intravenous contrast dye, a V/Q scan is used. A normal lung scan effectively excludes the diagnosis of PE, but only 25% of patients with suspected PE have a normal scan. In one of the largest studies evaluating V/Q scanning, the PIOPED II trial, V/Q scans could effectively rule-out PE in patients with a very low probability scan and a very low clinical likelihood of PE [12]. Other additional tests such as EKG or echocardiography may help with the diagnosis. However, EKG findings are often non-specific, as tachycardia is frequent. Evidence of right heart strain on EKG or echocardiography may support the diagnosis as well as provide information about the severity of the PE. One particular finding on echocardiogram, known as the McConnell's sign, is strongly suggestive of PE. In those patients with suspected PE and right ventricular dysfunction, the finding of normal wall motion of the RV apex but akinesia of the mid-RV free wall has a positive predictive value of 71% for the diagnosis of PE and a negative predictive value of 96%[13].

Treatment:

In hemodynamically stable patients, without contraindications to systemic anticoagulation, parenteral anticoagulation with subsequent conversion to vitamin K antagonists is the mainstay of therapy. Early initiation is paramount as patients may quickly decompensate. Patients who present to the emergency room with acute PE have decreased mortality if anticoagulation treatment commences in the emergency room, rather than waiting until after admission [14]. Supportive care of hypoxemia and hemodynamic instability should be instituted. Hemodynamically unstable patients may benefit from fibrinolytic therapy. However, the role for fibrinolysis is limited, with significant bleeding occurring in up to 13% of patients. The use of bolus thrombolytics during cardiopulmonary arrest may have some benefit when PE is strongly suspected[15][16] and the patient does not respond to resuscitation. Mechanical thrombolysis with catheter-directed embolectomy and fibrinolytic therapy can also be used. Systemic heparin, either in the form of unfractionated heparin or low-molecular-weight heparin (LMWH), is the mainstay of treatment. LMWH is advantageous in ease of administration, monitoring, lower potential for heparin-induced thrombocytopenia. However, it is not an appropriate choice for patients with renal failure or for patients at significant risk of bleeding, because of its longer half-life and lack of reversibility. Newer options for anticoagulation include oral factor Xa inhibition with agents under investigation, such as rivaroxaban [17, 18]. If patients continue to have PEs despite therapeutic anticoagulation, experience bleeding events, or have other contraindications to anticoagulation, permanent or temporary inferior vena cava filters (IVCF) may be used. IVCF can prevent further pulmonary emboli in patients with lower extremity deep venous thrombosis, but do not reduce mortality. Propagating ilio-femoral venous thrombus while on anticoagulation is another indication for IVCF placement.

CONCLUSION

Pulmonary embolism is a life-threatening condition affecting all age group of people. Venous thromboembolism and PE remain preventable causes of morbidity and mortality. By combining patient presentation, clinical suspicion, and scoring systems, diagnosis may be streamlined and unnecessary treatment may be minimized.PA is generally considered to be the most definitive test for the diagnosis of PE. More physicians have training and access to portable ultrasound devices, which may prevent delays in recognition and treatment of VTE. In-hospital patients, especially those who are critically ill, continue to pose diagnostic dilemmas. In such patients, clinical scoring systems and imaging may be inconclusive. Various diagnostic modalities have been suggested by various authors and it may be helpful to refer to one for a diagnostic strategy.

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