Pulmonary Embolism

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Venous thromboembolism (VTE), which encompasses deep venous thrombosis (DVT) and pulmonary embolism (PE),

Pulmonary Embolism : Occlusion of a pulmonary artery(ies) by a blood clot. Results from DVTs that have broken off and travelled to the pulmonary arterial circulation. PE is one of the leading causes of preventable deaths in hospitalized patients. It is one of the three major cardiovascular causes of death, along with myocardial infarction and stroke.

Thrombosis commonly occurs after periods of immobilization, but it can occur in normal individuals for no obvious reasons.

The majority (80%) of pulmonary emboli arise from the propagation of lower limb DVT .

Rare causes include septic emboli (from endocarditis affecting the tricuspid or pulmonary valves), tumor (especially choriocarcinoma), fat, air, amniotic fluid and placenta .

A variety of Risk Factors:

-Prior DVT or PE
-Estrogen, OCP, HRT
-Pregnancy
-Lower limbs injury
- Orthopedic Surgery
-Surgery requiring > 30 minutes general anesthesia
-Prolonged immobilization, travel abroad
-Malignancy
-Obesity
-Smoking
-Severe sepsis
-Congestive Heart Failure
-Age > 40
-Factor V Leiden mutation
-Protein C deficiency
-Protein S deficiency
-Antithrombin deficiency
-Prothrombin G20210A mutation
-Anticardiolipin antibodies, APS
-SLE,
-Hyperhomocystinemia

Pathophysiology:

When venous thrombi are dislodged from their site of formation they embolize to the pulmonary arterial circulation or, paradoxically, to the arterial circulation through a patent foramen ovale or atrial septal defect. About one-half of patients with pelvic vein thrombosis or proximal leg DVT develop PE, which is often asymptomatic.

The most common gas exchange abnormalities are hypoxemia (decreased arterial PO2) and an increased alveolar-arterial O2 tension gradient, which represents the inefficiency of O2 transfer across the lungs. ↓PaCO2 due to tachypnea.

Right-Ventricular (Rv) Dysfunction :Progressive right heart failure is the usual cause of death from PE.

P.E. Clinical features:

VTE can be difficult to diagnose. It is helpful to consider Clinical presentation varies, depending on number, size and distribution of emboli and on underlying cardiorespiratory reserve .

Through history taking consider the following :

-Is the clinical presentation consistent with PE?
-Does the patient have risk factors for PE?
-Are there any alternative diagnoses that can explain the patient's presentation?

DVTs often present with progressive lower calf discomfort. For PE, dyspnea is the most common presenting symptom. Chest pain, cough, or hemoptysis can indicate pulmonary infarction with pleural irritation. Syncope can occur with massive PE.

Acute Massive PE:

Hemodynamic effects:→↓cardiac output, acute right heart failure.

Symptoms → Faintness or collapse, crushing central chest pain, apprehension and sever dyspnea .

Signs →Major circulatory collapse: tachycardia, hypotension, ↑JVP, RV gallop rhythm ,loud P2, sever cyanosis , ↓urinary output.

Chest X-ray →Usually normal. May be subtle oligaemia.

ECG → S1Q3T3 anterior T-wave inversion, RBBB and right axis deviation.

Arterial blood gases→ Markedly abnormal with ↓PaO2 and ↓PaCO2.metabolic acidosis.

Alternative diagnoses→ Myocardial infarction, pericardial tamponade ,aortic dissection.

Acute small/medium PE:

Hemodynamic effects:→ Occlusion of segmental pulmonary artery → infarction + effusion

Symptoms → Pleuritic chest pain, restricted breathing and hemoptysis.

Signs→ Tachycardia, pleural rub, raised hemidiaphragm، crackles , effusion (blood stain),fever.

Chest X-ray → Pleuropulmonary opacities, pleural effusion, linear shadows, raised hemidiaphragm

ECG → Sinus tachycardia.

Arterial blood gases → May be normal or ↓PaO2 or ↓PaCO2.

Chronic PE:

Hemodynamic effects:→ Chronic occlusion of pulmonary microvasculature , right heart failure.

Symptoms → Exertional dyspnea. Late symptoms of pulmonary hypertension or right heart failure.

Signs → May be minimal early in disease. Later: RV heave,loud P2 ,signs of Rt heart failure

Chest X-ray → Enlarged pulmonary artery trunk, enlarged heart **,**prominent Rt ventricle

ECG → RV hypertrophy and strain

Arterial blood gases → Exertional ↓PaO2 or desaturation on formal exercise testing .

Probability scoring for diagnosing pulmonary embolism :

Simplified Wells score for pulmonary embolism:

- ***Previous pulmonary embolism or DVT 1***
- ***Immobilization or major surgery in previous 4 weeks 1.5***
- ***Cancer 1.5***
- ***Hemoptysis 1.5***
- ***Heart rate more than 100 bpm 1.5***
- ***Sign of DVT 3***
- ***Alternative diagnosis is less than pulmonary embolism 3***

TOTAL SCORE:

0---1 point = Low probability

2----6 point = Moderate probability

7 or more = High probability

P.E. Investigations:

ECG :is often normal but is useful in excluding other important differential diagnoses, such as acute myocardial infarction and pericarditis. The most common findings in PE include sinus tachycardia ,AF, anterior T-wave inversion but these are non-specific; larger emboli may cause right heart strain revealed by an S1Q3T3 pattern, ST-segment and T-wave changes, or the appearance of right bundle branch block and right axis deviation .

Arterial blood gases(ABG): typically show a reduced PaO2 and a normal or low PaCO2, and an increased alveolar– arterial oxygen gradient, Metabolic acidosis.

D-dimer :is a Sensitive but not specific , Up to 80% of ICU patients have elevated D- dimer in the absence of VTE

Normal D-dimer level (<500 μg/mL by enzyme-linked immunosorbent assay) essentially rules out PE in pts with low-to-moderate risk .

Other lab test such as CBC, Coagulation profile, ESR, LDH

Chest X-ray is most useful in excluding key differential diagnoses, e.g. pneumonia or pneumothorax

- ❖ PE signs in x ray :
- Pulmonary opacities (any size or shape, rarely lobar or segmental, can cavitate).
- Elevated hemidiaphragm.
- Horizontal linear opacities(bilateral and usually in lower zones).
- Pleural effusion.
- Wedge-shaped opacity.
- Oligaemia of lung field.
- Enlarged pulmonary artery.

Color Doppler ultrasound of the leg veins remains the investigation of choice in patients with suspected DVT.

Echocardiography bedside ECHO is extremely helpful to rule out left ventricular abnormalities and valvular heart disease. and in the differential diagnosis and assessment of acute circulatory collapse.

CT pulmonary angiography (CTPA): is the diagnostic test. It has the advantage of visualizing the distribution and extent of the emboli. The sensitivity of CT may be increased by simultaneous visualisation of the femoral and popliteal veins. As contrast may be nephrotoxic, care should be taken in patients with renal impairment and the use of iodinated contrast media should be avoided in those with a history of allergy to it.

Conventional pulmonary angiography has been largely superseded by CTPA but is still useful in selected settings or to deliver catheter-based therapies.

Ventilation-perfusion scanning:

- is less commonly used, as its utility is limited in patients with pre-existing chronic cardiopulmonary pathology and the scan is most frequently regarded as indeterminate.
- The scan may reveal focal areas of hypoperfusion,
- Ventilation-perfusion scan findings absence of perfusion due to severe, asymmetrical involvement. The type of defect may vary depending on the size and location of the involved veins.

Differential Diagnosis of P.E.:

- Acute coronary syndrome ,dissected aortic aneurysm
- Congestive heart failure, Pericarditis
- Pneumonia, asthma, chronic obstructive pulmonary disease
- Pleurisy: "viral syndrome," costochondritis, musculoskeletal discomfort
- Rib fracture, pneumothorax
- Anxiety.

Management:

General measures

Sufficient oxygen should be given to hypoxaemic patients to maintain arterial oxygen saturation above 90% .

•Circulatory shock should be treated with intravenous fluids or plasma expander.

•External cardiac massage may be successful in the moribund patient by dislodging and breaking up a large central embolus

Anticoagulation: Immediate full anticoagulation is mandatory for all patients suspected of having DVT or pulmonary embolism. Diagnostic investigations should not delay empirical anticoagulant therapy.

Heparin reduces further propagation of clot and the risk of further emboli, and lowers mortality. It is most easily administered as Unfractionated heparin therapy UFH IV , or subcutaneous low molecular weight heparin (LMWH)

- If IV UFH is chosen, an initial bolus of 80 U/kg or 5000 U followed by an infusion of 18 U/kg/h or 1300 U/h should be given, with the goal of rapidly achieving and maintaining the aPTT at levels that correspond to therapeutic heparin levels. Fixed-dose and monitored regimens of subcutaneous UFH are available and are acceptable alternatives.
- critical therapeutic level of heparin is 1.5 times the baseline control value or the upper limit of normal range of the activated partial thromboplastin time (aPTT).
- protamine sulfate is antidote to UFH

The dose is based on the patient's weight and there is usually no requirement to monitor tests of coagulation.

Treatment with LMWH should continue for at least 5 days, during which time an oral anticoagulant is commenced. Fondaparinux, a synthetic pentasaccharide closely related to heparin, represents an alternative to LMWH .

Warfarin – a vitamin K antagonist – remains the most commonly used oral anticoagulant.

PT should be measured on a regular basis; the goal is an INR of 2-3.

Vit k is antidote to warfarin.

Patients may have treatment initiated using concomitant warfarin and unfractionated heparin for 5 days in the hospital, with discharge on warfarin alone when the international normalized ratio (INR) is 2. Alternatively, patients may be discharged on concomitant therapy with a LMWH and warfarin for at least 5 days. The LMWH is then discontinued in the outpatient setting when the INR reaches 2.

Warfarin Therapy is initiated with a high loading dose, followed by a maintenance dose based on the international normalized ratio(INR).
LMWH should not be discontinued until the INR is 2 or more for at least 24 hours .
Due to the narrow therapeutic index of warfarin and its propensity to interact with other drugs and food, regular measurement of the INR is required throughout the duration of anticoagulation.
Decisions regarding the duration of anticoagulation represent a balance between the risk and consequences of recurrence, and the risks of prolonged anticoagulation.

Direct thrombin inhibitors and factor Xa inhibitors:

Newer thrombin inhibitors or activated factor X inhibitors offer more predictable dosing and have no requirement for coagulation monitoring; they may ultimately replace warfarin .
Apixaban, dabigatran, rivaroxaban, and edoxaban are alternatives to warfarin for prophylaxis and treatment of PE. Apixaban, edoxaban, and rivaroxaban inhibit factor Xa, whereas dabigatran is a direct thrombin inhibitor.

Rivaroxaban.

Rivaroxaban (Xarelto) is an oral factor Xa inhibitor approved by the FDA in November 2012 for the treatment of DVT or PE, and to reduce risk of recurrent DVT and PE following initial treatment.

Dabigatran.

Dabigatran (Pradaxa) was approved by the FDA in 2014 for the treatment of DVT and PE and reducing venous thromboembolic recurrence.
In patients with an identifiable and reversible risk factor, anticoagulation may be safely discontinued following3 months of therapy .
Those with persistent prothrombotic risks or a history of previous emboli should be anticoagulated for life.
In patients with cancer associated VTE, LMWH should be continued for at least 6 months before switching to warfarin .
For patients with unprovoked VTE, the appropriate duration of anticoagulation should be at least 3 months.

Fibrinolysis(Thrombolytic)tPA:

- Massive PE causing hemodynamic instability (shock and/or low blood pressure, defined as a systolic blood pressure <90 mmHg
- This is an indication for thrombolysis, the enzymatic destruction of the clot with medication. In this situation, it is the best available treatment in those without contraindications.
- Thrombolytic time window in Pulmonary embolism is 2 weeks , while in AMI , CVA is more shorter .
- Successful fibrinolytic therapy rapidly reverses right heart failure and may result in a lower rate of death and recurrent PE by :

(1) dissolving much of the anatomically obstructing pulmonary arterial thrombus
(2) preventing the continued release of serotonin and other neurohumoral factors that exacerbate pulmonary hypertension,

(3) lysing much of the source of the thrombus in the pelvic or deep leg veins, thereby decreasing the likelihood of recurrent PE.
The preferred fibrinolytic regimen is 100 mg of recombinant tissue plasminogen activator (tPA) administered as a continuous peripheral intravenous infusion over 2 hours .

Contraindications to fibrinolysis include

Intracranial disease
Active GIT bleeding
Bleeding disorders
Recent surgery
Trauma
The overall major bleeding rate is about 10%, including a 1–3% risk of intracranial hemorrhage.

Pulmonary Embolectomy:

The risk of intracranial hemorrhage with fibrinolysis has prompted a renaissance of surgical embolectomy. More prompt referral before the onset of irreversible cardiogenic shock and multisystem organ failure and improved surgical technique have resulted in a high survival rate. A possible alternative to open surgical embolectomy is catheter embolectomy.

Inferior Vena Caval (IVC) Filters:

The two principal indications for insertion of an IVC filter are
(1) Active bleeding that precludes anticoagulation.
(2)Recurrent venous thrombosis despite intensive anticoagulation.

VTE and pregnancy

Maternal mortality: VTE is the leading cause.
CTPA: may be performed with fetal shielding. It is important to consider the risk of radiation to breast tissue (particularly if there is a family history of breast carcinoma) and the risk of iodinated contrast media to mother and fetus (neonatal hypothyroidism.(
V_ / Q_ scanning: greater radiation dose to fetus but less to maternal breast tissue.
• Warfarin: teratogenic, so VTE should be treated with LMWH during pregnancy.

DVT prevention:

The use of elastic compression stockings provides a safe and effective adjunctive treatment
Early ambulation is recommended over bed rest when feasible

Pulmonary Hypertension:

Defined as a mean pulmonary artery pressure > 25 mmHg at rest or 30 mmHg with exercise. Although respiratory failure due to intrinsic pulmonary disease is the most common cause of pulmonary hypertension, severe pulmonary hypertension may occur as a primary disorder, as a complication of connective tissue disease (e.g. systemic sclerosis), or as a result of chronic thromboembolic events.
The increased pulmonary artery (PA) pressure found in PAH is due to disturbances in key vascular mediator pathways including relative deficiencies of vasodilators such as nitric oxide (NO) and prostacyclin, as well as exaggerated production of vasoconstrictors such as endothelin and

thromboxanes. Given the generally accepted role of pulmonary vasoconstriction in PAH, vasodilators such as bosentan, epoprostenol, iloprost, and sildenafil are a natural initial therapeutic choice.

Clinical Features:

Presentation is insidious and is often diagnosed late .

As a result, PH is often not suspected until symptoms become severe or serious. It has been estimated that more than 20% of patients have symptoms of PH for longer than two years before it is recognized.

Typical symptoms include breathlessness, chest pain, fatigue, palpitation and syncope.

Important signs:

Elevation of the JVP (with prominent ‘a’ wave if in sinus rhythm),Parasternal heave (RV hypertrophy)

Accentuation of P2

Right ventricular third heart sound.

Investigations:

Chest x-ray findings:

Enlarged pulmonary arteries

Peripheral pruning

Right ventricular enlargement

ECG may show: right ventricular strain pattern

Confirmation: **transthoracic Echocardiography**; Doppler assessment of the tricuspid regurgitant jet provides a non-invasive estimate of the pulmonary artery pressure .

Further assessment in specialist centres that can perform **right heart catheterization** to assess pulmonary haemodynamics and measure vasodilator responsiveness, to guide further therapy.

Management:

Pulmonary hypertension is incurable but new treatments can improve exercise performance, symptoms and prognosis .

All patients should receive :

-Warfarin with INR target (2-3)

-O2 if patient hypoxic

The use of diuretics and digoxin can help relieve symptoms of right heart failure.

Specific treatment options include

High-dose Calcium Channel blocking drugs (CCBs).

Prostaglandins such as epoprostenol (prostacyclin) or iloprost therapy

Sildenafil : phosphodiesterase (PDE) inhibitors

oral endothelin antagonist bosentan .

Selected patients can be referred for heart-lung transplantation, and pulmonary thromboendarterectomy may be contemplated in those with chronic proximal pulmonary thromboembolic disease.

Atrial septostomy (the creation of a right to left shunt) decompresses the right ventricle and improves haemodynamic performance at the expense of shunting and hypoxaemia.