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Update on the diagnosis and treatment of pulmonary embolism

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Abstract

Background: The pulmonary embolism is a frequent cardiovascular syndrome associated with a high mortality and important medical costs.

Objective and Method: The purpose of this short review is to update clinicians' knowledge on the diagnosis and management of patients with pulmonary embolism.

Results: The predisposing factors for pulmonary embolism can be classified into three groups according to their importance. The main cause of death is the acute right ventricular failure due to acute increase in pressure. The symptomatology of pulmonary embolism is highly varied, ranging from asymptomatic patients to those presenting with major hemodynamic instability and shock. The diagnosis of pulmonary embolism is based on three essential factors: clinical elements summarized by various validated scores, D-Dimer assays and imaging methods. The emergency nature of treatment depends on the assessment of hemodynamic stability. Severe forms presenting with hemodynamic instability or cardiac arrest require immediate treatment with thrombolysis or surgical/percutaneous embolectomy if thrombolysis is contraindicated. Other supportive measures include empirical anticoagulation based on clinical suspicion, and respiratory/cardiovascular support.

Conclusion: Pulmonary embolism remains a frequent and serious disease. This brief summary provides an update on the management of patients suffering from pulmonary embolism. Its aim is to help clinicians to accurately diagnose and manage this group of patients.

Update on the diagnosis and treatment of pulmonary embolism

Venous thromboembolism, clinically presented as deep vein thrombosis (DVT or pulmonary embolism (PE), is the third most frequent acute cardiovascular syndrome, after myocardial infarction and cerebrovascular accident. The annual incidence of pulmonary embolism ranges from 40-120 per 100,000 inhabitants with a mortality of 14% (in-hospital) and 20% in 90 days. The incidence of deep venous thrombosis (DVT) is 53-162 per 100,000 inhabitants and is eight times higher in individuals aged ⩾80 years compared to the fifth decade of life. The cost of these diseases in the EU amounts to €8.5 billion. Pulmonary embolism causes 300,000 deaths annually in the US. The mortality rate of cases with acute pulmonary embolism may be decreasing, while diagnosis is increasing.[1]

Factors predisposing the venous thromboembolism

It is well known that thrombus formation is facilitated by 3 factors (Virchow's triad): venous stasis, local hypercoagulation and endothelial damage. There are many predisposing factors of venous thromboembolism that can be classified into three groups according to importance:[2]

1. Strong risk factors : fractures of the lower limbs, hospitalization for heart failure or atrial fibrillation (within the previous 3 months), hip or knee prosthesis, major trauma, myocardial infarction (within 3 months), previous thrombosis, spinal cord injury.

2. Moderate risk factors : arthroscopic knee surgery, autoimmune diseases, blood transfusion, central venous lines, intravenous catheters, chemotherapy, congestive heart failure or respiratory failure, erythropoiesis stimulating agents, hormone replacement therapy (depends on formulation), fertilization in vitro, therapy with oral contraceptives, postpartum period, infection (especially pneumonia, urinary tract infection and HIV), inflammatory bowel disease, cancer (highest risk in metastatic disease), paralytic stroke, superficial venous thrombosis, thrombophilia.

3. Weak risk factors: bed rest > 3 days, diabetes mellitus, arterial hypertension, immobility due to sitting (e.g. prolonged car or plane travel), old age, laparoscopic surgery (e.g. Cholecystectomy), obesity, pregnancy, varicose veins.

Pathophysiology of heart failure from pulmonary embolism.

Acute right ventricular failure due to acute increase in pressure is considered the main cause of death. The right ventricle does not have the capacity to withstand an actual significant increase in intraventricular pressure and this leads to expansion of the ventricular cavity. Pulmonary arterial pressure (PAPm) increases if > 30-50% of the arterial bed is occluded by thrombi. Hypoxic vasoconstriction in the affected lung area leads to an increase in pulmonary vascular resistance. Right ventricular enlargement alters the contractile properties of the right ventricle via the Frank-Starling mechanism. Immediate adaptation is limited, the unaccustomed right ventricle with thin walls is unable to generate a PAPm >40 mmHg. As a result, an imbalance between supply and demand for O_2 in the right ventricle is created, coronary hypoperfusion occurs which leads to major hemodynamic compression, cardiogenic shock and death.[3]

Clinical forms of pulmonary embolism vary. Undoubtedly, the form that requires immediate diagnosis and treatment is severe pulmonary embolism. Severe or high-risk pulmonary embolism manifests with hemodynamic instability and includes the following clinical forms:[1]

- The most severe form presents as cardiac arrest and requires cardio-pulmonary resuscitation.

- The form that manifests as obstructive shock after adequate vascular filling and is defined by systolic pressure <90 mmHg or requires the use of vasopressors to maintain a systolic arterial pressure ≥90 mmHg.

- Persistent hypotension over 15 minutes and excluding another cause of hypotension such as arrhythmia, hypovolemia or sepsis.

Symptomatology of pulmonary embolism

The symptomatology of pulmonary embolism is very diverse and can range from an asymptomatic patient to forms with major hemodynamic instability and shock. Very often it manifests with clinical signs and non-specific symptoms such as dyspnea, chest pain (frequent, caused by pleural irritation), syncope (17% of cases), hemoptysis, hemodynamic instability or being completely asymptomatic (accidental diagnosis).[4]

Other signs of pulmonary embolism include hypoxia (⩽40% of patients have normal SaO_2), hypocapnia, tachycardia. Pulmonary radiography is often abnormal and nonspecific (excluding other causes of dyspnea or chest pain). In the ECG, we often find negative T waves in leads V1–V4, QR aspect in V1, S1Q3T3 and right bundle branch block. In patients with severe pulmonary

embolism, 1/3 of patients create an intracardiac shunt from right to left through the opening of the foramen ovale, which manifests with severe hypoxemia and in some cases with cerebral vascular accident from paradoxical embolism.[5]

Diagnosis of pulmonary embolism

Standard diagnostic strategies for pulmonary embolism consist of 3 steps: assessment of clinical probability, D-Dimer dosing, and imaging. Among the most used clinical tables that take into account the clinical elements for diagnosis are that of the revisited Geneva system; the PERC system; the Wells system.[6] All these tools account for clinical elements that are responsible for the risk of pulmonary embolism including: previous history of thrombosis/pulmonary embolism; tachycardia, surgery or fracture of the extremities in the past month; hemoptysis; active cancer; unilateral leg pain and edema; and age. The more clinical elements are present, the higher the probability of pulmonary embolism.

D-Dimers has very good negative predictive value. A normal D-Dimer level excludes EP or acute DVT. In cases where D-Dimer values are positive, their value is predictive because increased values are found in patients with malignant disease; hospitalized patients; pregnancy; severe infection and inflammation after having pulmonary embolism or deep thrombosis. The most commonly used test is ELISA and has a diagnostic sensitivity of ⩾95% to exclude EP in patients with low or intermediate probability.[7]

Imaging methods confirm or exclude the diagnosis of pulmonary embolism. Computerized tomographic pulmonary angiography (spiral scan) is most used method in clinical practice. It enables the visualization of pulmonary arteries up to the sub-segmental level with 83% sensitivity and 96% specificity. The shortcoming of this technique is that it does not visualize the subsegmental vascular network and that further methods are needed in case of inconsistency between the clinical judgment and the negative result.[7] Another important technique is pulmonary scintigraphy, which is a very accurate diagnostic test. It is used in patients with a low level of clinical probability, young patients (especially women), pregnant women, in patients with a history of contrast-induced anaphylaxis, and patients with severe renal insufficiency. Pulmonary angiography is the "gold standard" for diagnosis or exclusion of diagnosis. It enables visualization of thrombi as small as 1-2 mm within sub-segmental arteries. It is a difficult and invasive technique with a mortality of 0.5%, non-fatal complications of 1% and 5% for small complications. Echocardiography is another very important diagnostic technique, frequently used in clinical practice. It provides very important indirect data such as signs of right ventricular overload and dysfunction and is very important in cardiogenic shock. The fact that it can it is transported to the patient's bed, which is not harmful and which is available at any time, makes this technique more used. In cases of hemodynamic instability, if there is no right ventricular dysfunction, echocardiography excludes severe pulmonary embolism. If there is dysfunction of the right ventricle, then the diagnosis must be verified with a scanner if it is available. If the scanner is not available, clinicians must proceed directly to the treatment of severe pulmonary embolism.[8]

Treatment of pulmonary embolism

The urgency of treatment depends on the assessment of hemodynamic stability. Most patients with EP are hemodynamically stable at presentation.[9] The initial approach should focus on general supportive measures while the diagnostic evaluation is ongoing. Supportive measures include the following: peripheral intravenous access with or without IV fluids, administration of oxygen, and empiric anticoagulation depending on clinical suspicion of EP, risk of bleeding, and expected timing of definitive diagnostic tests. Severe cases with major hemodynamic instability, shock or cardiac arrest require systemic thrombolysis or surgical/percutaneous embolectomy in case of thrombolysis contraindications. Among the most used thrombolytics are rtPA; streptokinase and urokinase. Care must be taken in absolute and relative contraindications to the use of fibrinolytics. In case of major hemodynamic insufficiency, inotropes and vasopressors should be used for the purpose of hemodynamic stabilization. The most severe cases require hemodynamic/respiratory mechanical support through extracorporeal membrane oxygenation (ECMO) by selecting the patients appropriately. All cases of pulmonary emboli and DVT require immediate anticoagulation. In patients with high or intermediate clinical probability, parenteral anticoagulation should be initiated pending the results of diagnostic tests. Anticoagulation can be done with unfractionated heparin (UFH), low molecular weight heparin (LMWH) or Fondaparinux. Milder cases can be treated directly with direct oral anticoagulants such as Rivaroxaban, Apixaban, Endoxaban or Dabigatran. Antivitamins K can also

be used for anticoagulation after the acute phase. Percutaneous embolectomy enables mechanical reperfusion by inserting a catheter into the pulmonary arteries via the femoral vein, fragmentation, aspiration of the thrombus, or more often with reduced-dose in situ thrombolysis. Surgical embolectomy is usually performed with cardiopulmonary bypass, without aortic clamping and cardioplegia. It consists in opening the two main pulmonary arteries and removing and aspiration of thrombi.[10] This treatment remains a good therapeutic option, notably in experienced centers and applied to patients with unstable hemodynamics who cannot benefit from thrombolytic therapy. In extreme cases, initial hemodynamic stabilization requires the use of VA-ECMO, and the patient may then undergo surgical embolectomy. This procedure allows better postoperative recovery of right ventricular function.[11]

Trauma patients are at increased risk of developing thromboembolic complications. Preventing thrombotic events after trauma remains a very important therapeutic component. A very critical issue is the timing of the initiation of anti-thromboembolic therapy. Many surgical trauma centers have developed their own guidelines. In order to standardize and optimize thromboembolic prophylaxis, the American Association for the Surgery of Trauma and the American College of Surgeons-Committee on Trauma have published their valuable recommendations for adult patients in all centers treating traumatized patients.[12]

Conclusion

Venous thromboembolism is a frequent acute cardiovascular syndrome. Clinicians need to be well informed about the predisposing factors, pathophysiology and diagnostic tools of pulmonary embolism. Appropriate management of pulmonary embolism based on clinical presentation and supported by didactic algorithms can save the lives of many patients.

References

1. Konstantinides SV, Meyer G. The 2019 ESC Guidelines on the Diagnosis and Management of Acute Pulmonary Embolism. *Eur Heart J* 2019;40(42):3453-55. doi: 10.1093/eurheartj/ehz726 [published Online First: 2019/11/08]

2. Rogers MA, Levine DA, Blumberg N, et al. Triggers of hospitalization for venous thromboembolism. *Circulation* 2012;125(17):2092-9. doi: 10.1161/CIRCULATIONAHA.111.084467 [published Online First: 2012/04/05]

3. Konstantinides SV, Torbicki A, Agnelli G, et al. 2014 ESC guidelines on the diagnosis and management of acute pulmonary embolism. *Eur Heart J* 2014;35(43):3033-69, 69a-69k. doi: 10.1093/eurheartj/ehu283 [published Online First: 2014/09/01]

4. Prandoni P, Lensing AW, Prins MH, et al. Prevalence of Pulmonary Embolism among Patients Hospitalized for Syncope. *N Engl J Med* 2016;375(16):1524-31. doi: 10.1056/NEJMoa1602172 [published Online First: 2016/11/01]

5. White RH. The epidemiology of venous thromboembolism. *Circulation* 2003;107(23 Suppl 1):I4-8. doi: 10.1161/01.CIR.0000078468.11849.66 [published Online First: 2003/06/20]

6. Freund Y, Cachanado M, Aubry A, et al. Effect of the Pulmonary Embolism Rule-Out Criteria on Subsequent Thromboembolic Events Among Low-Risk Emergency Department Patients: The PROPER Randomized Clinical Trial. *JAMA* 2018;319(6):559-66. doi: 10.1001/jama.2017.21904 [published Online First: 2018/02/17]

7. Perrier A, Roy PM, Aujesky D, et al. Diagnosing pulmonary embolism in outpatients with clinical assessment, D-dimer measurement, venous ultrasound, and helical computed tomography: a multicenter management study. *Am J Med* 2004;116(5):291-9. doi: 10.1016/j.amjmed.2003.09.041 [published Online First: 2004/02/27]

8. 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(7511):259. doi: 10.1136/bmj.331.7511.259 [published Online First: 2005/07/30]

9. Kahn SR, de Wit K. Pulmonary Embolism. *N Engl J Med* 2022;387(1):45-57. doi: 10.1056/NEJMcp2116489 [published Online First: 2022/07/07]

10. Helms J, Carrier M, Klok FA. High-risk pulmonary embolism in the intensive care unit. *Intensive Care Med* 2023;49(5):579-82. doi: 10.1007/s00134-023-07011-0 [published Online First: 2023/03/18]

11. Goldberg JB, Spevack DM, Ahsan S, et al. Survival and Right Ventricular Function After Surgical Management of Acute Pulmonary Embolism. *J Am Coll Cardiol* 2020;76(8):903-11. doi: 10.1016/j.jacc.2020.06.065 [published Online First: 2020/08/21]

12. Yorkgitis BK, Berndtson AE, Cross A, et al. American Association for the Surgery of Trauma/American College of Surgeons-Committee on Trauma Clinical Protocol for inpatient venous thromboembolism prophylaxis after trauma. *J Trauma Acute Care Surg* 2022;92(3):597-604. doi: 10.1097/TA.0000000000003475 [published Online First: 2021/11/20]